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# The Goulstonian Lectures

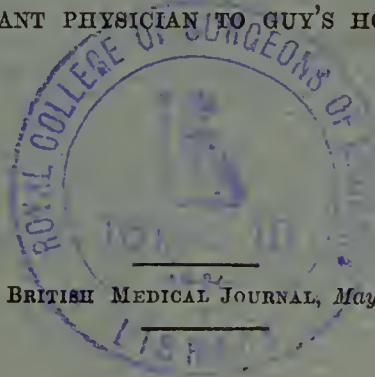
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## Influence of Pregnancy upon Certain Medical Diseases, and of Certain Medical Diseases upon Pregnancy.

*DELIVERED BEFORE THE ROYAL COLLEGE OF PHYSICIANS  
OF LONDON,*

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THE INFLUENCE OF PREGNANCY UPON  
CERTAIN MEDICAL DISEASES, AND OF  
CERTAIN MEDICAL DISEASES  
UPON PREGNANCY.

LECTURE I.

INTRODUCTION.

MR. PRESIDENT AND GENTLEMEN,—The title of these lectures perhaps requires a few words of explanation, in case it might be at all misleading. The subjects that it is proposed to discuss will not be dealt with from an obstetrical point of view, but purely from their medical or pathological aspect. The gynaecologist and the obstetrician must naturally be interested in the medical diseases which may arise in a pregnant woman, and in some cases the treatment in these circumstances may be gynaecological or obstetrical rather than medical. I have not the ability to deal with gynaecological or obstetrical treatment, and shall therefore say nothing about it. On the other hand, the fact that a medical disease arises, or is already present, when a patient has become pregnant by no means necessarily implies that the immediate treatment of the patient should be carried out from a gynaecological or obstetrical standpoint. It is true that there are conditions under which the aid of the obstetric physician may be required to terminate the pregnancy artificially, and it is also true that similar aid will be essential when the pregnancy reaches its natural term, or earlier if any accidental termination to it should arise. There are, however, many conditions in which the pregnancy may be, as it were, an accidental concomitant or complication of the medical disease; there are other conditions in which pregnancy is actually the cause of the medical disease, and many of these cases are of direct interest to the physician.

If in a given case it should be decided that the pregnancy may be allowed to run its natural course, the responsibility for the patient's health would rest with the physician until such time as the pregnancy either reached its term or ceased to be itself normal. It is, therefore,

essential that the physician should be fully acquainted with the probable effects both of the pregnancy upon the medical disease from which the patient may be suffering and also of the medical disease upon the pregnancy. Two examples may, perhaps, assist this explanation. Suppose, for instance, that a pregnant woman contracts typhoid fever. Three questions at once arise—namely, Is the fact that this patient is pregnant likely to make the typhoid fever more severe than it otherwise would be? Is the patient's pregnancy likely to terminate abnormally on account of the typhoid fever? Ought the treatment of this patient to be different in any way from that of other persons suffering from typhoid fever? It is clear that, so far at least as the typhoid fever is concerned, the treatment should be carried out by those most familiar with typhoid fever if it can be shown that the treatment of such cases ought to be upon the same lines as that of non-pregnant persons suffering from the disease. So far as the typhoid fever is concerned the pregnancy may be an accidental concomitant, but it is important to the physician to know what is likely to be the result of the combination.

As my second example, may I take that of a patient who presents herself with that peculiar skin eruption, herpes gestationis? If she were not pregnant she would not have the eruption; but, having the eruption, the immediate treatment of the patient for her skin trouble is probably best carried out by one who is most familiar with skin diseases, provided it is known that the pregnancy is not likely to run an abnormal course.

It is only from the medical point of view that I am in a position to discuss the mutual effects of pregnancy and medical diseases; and seeing that there are few medical diseases that cannot either themselves arise during pregnancy or else permit of pregnancy occurring when they are already in existence, it is clear that the whole field cannot be covered in three lectures. I am obliged, therefore, to restrict the discussion to a few affections which appear to possess particular interest.

In the first place, there are certain medical diseases for which pregnancy appears to be itself directly responsible. One of the most definite of these, comparatively rare no doubt, yet full of interest from a pathological point of view, is

#### HERPES GESTATIONIS.

This disease is apparently related to pemphigus, to hydroa, to erythema bullosum, and to dermatitis herpetiformis or Dühring's disease. The eruption is variable in the extent to which erythematous patches, pinkish-red papules, and wheals not unlike those of urticaria are present, but to whatever degree these may coexist the distinctive lesion is vesicular or bullous. Sometimes the blebs are comparatively large and widely separated, and they are preceded by more or less erythema, in which case the eruption is very similar to that of erythema



bullosum. More rarely the bullae occur before any erythema is obvious and pemphigus is simulated. In other cases, again, the vesicles are smaller, and they may be arranged in groups upon an inflamed base like those of herpes zoster—the herpetiform variety. The cases that I have seen have exhibited a mixed condition, the majority of the vesicles being only moderate in size, with here and there amongst them a few that were large enough to be called bullae. The smaller vesicles have shown a slight tendency to be grouped together as in herpes, but it is not often that they are confluent, or that a single group contains as many vesicles crowded together as is the case in well-marked herpes zoster. The vesicles, whether large or small, have been preceded by an itching erythema, which has in the beginning been smooth, but which has rapidly become first papular and then vesicular. The eruption itself has been more like that of dermatitis herpetiformis than anything else, the chief clinical distinction between the two being solely the direct relationship of herpes gestationis to pregnancy.

#### *An Illustrative Case.\**

The following is an illustrative case :

The patient, 41 years of age, was under the care of Sir Cooper Perry in Guy's Hospital, and was sufficiently ill to require treatment in bed for over a month. Her history was briefly this: She was the only member of her family troubled with the complaint. She had been perfectly well up to, and for some time after, her marriage, when she was 23 years old. She had had seven living children and four miscarriages. The first miscarriage occurred after she had had three living children, and it was then that she suffered from her skin trouble for the first time. Since then, though quite free from it between whiles, she had had the eruption with each successive pregnancy, the itching erythema, vesicles, and bullae recurring constantly upon her hands and arms and sometimes upon her trunk, legs, and feet. She was three months pregnant at the time of her admission to the hospital; one month previously her ninth attack of herpes gestationis began with pains and irritation on the hands and forearms, rapidly followed by the eruption of discrete water blisters of moderate size, which, owing to scratching, broke down and discharged clear fluid. Each bleb dried in and healed in about a week, leaving a reddish mark which was slow to fade, whilst fresh vesicles kept on appearing daily in the neighbourhood. There was no pyrexia and no marked constitutional disturbance beyond what could be attributed to broken sleep, the result of irritation in the affected areas of skin. The arms and hands had been involved for three weeks before vesicles developed elsewhere, and then without apparent cause a precisely similar eruption came out upon the face and ears, spreading thence to the chest, abdomen, buttocks, lower limbs, and feet. The number of blebs upon the trunk was never so great as that upon the limbs. Flexor and extensor surfaces were equally involved, and the parts were not only irritable but also painful. The

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\* See also C. A. Douglas Bryan, *Lancet*, June 4th, 1904, p. 1570, and numerous papers in the journals of dermatology.

pains were doubtless due, in part at least, to the sore places being made worse by scratching. Left to themselves the blebs healed without breach of surface and without pyoderma. Some of the vesicles that had been interfered with either bled or became pustular; the latter change was always consequent upon inoculation by scratching. There was no involvement of mucous membranes, though there are doubtless cases in which the buccal mucosa and the colon may be affected, as has been observed in some instances of erythema bullosum. Under treatment by the yellow oxide of mercury ointment externally and by Fowler's solution of arsenic internally, together with rest in bed, light diet, and laxatives, there was some abatement in the skin trouble after about three weeks, but even during the continuance of the treatment a severe relapse ensued whilst the patient was still in the hospital. The trouble, waxing and waning in this way, persisted until the child was born, living, at term, and then, as on eight former occasions, the herpes gestationis rapidly got well by itself.

This case is fairly typical, and there are but few points to add before passing on to consider the pathology of the condition. It is not only possible for a patient like the above to have no trouble during the first pregnancies and then to develop the disease in later ones, but it is also possible that having had the skin disease in one pregnancy she may escape it at the next and yet develop it again in a later one. The time of onset is usually of the accelerating type—that is to say, in successive pregnancies it is likely that the date at which the herpes gestationis will reappear is a little earlier each time. It is, moreover, probable that the attacks will tend to become severer rather than the reverse. A few cases exhibit severe constitutional disturbance, with pyrexia and loss of appetite. It is, moreover, a curious fact that whereas the majority of the patients develop the trouble during pregnancy and lose it during the puerperium or soon after, it occasionally happens, as in another case under the care of Sir Cooper Perry, that the eruption first appears after labour, lasts a variable number of weeks or months, and then goes away spontaneously, not to reappear until just after another child has been born.\*

#### *Pigmentation.*

Another point that may be of interest perhaps is the increased pigmentation of the skin that is apt to be left after each attack. The pigmentation may be generalized all over the body in much the same way as it is in severe cases of Addison's disease. Usually, however, it is most marked in those parts of the skin in which the eruption itself has been worst. It is well known that uterine disorders are apt to cause pigmentation—the uterine chloasma—but this is, as a rule, much more marked upon the face, especially upon the forehead and around the eyes, than it is elsewhere. There is little or no evidence that the pigmentation which follows herpes gestationis

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\* For a case recurring at menstrual periods, see Douglas Bryan, loc. cit.

is in any way allied to uterine chloasma; indeed, there is seldom any obvious uterine derangement in the patients who suffer from it. The chief causes of the pigmentation are probably, first, the constant scratching or rubbing that the irritation in the affected parts gives rise to, just as it does in phthieriasis, where pigmentation also becomes well marked as time goes on; and secondly, the arsenic which is administered in most of the cases. The darkening of the skin is so great in some patients that they may look as if they might be of coloured extraction. There is apparently no record as to whether or not the pigmentation ever occurs upon the buccal mucosa as well as upon the skin, but between the attacks of herpes gestationis it would sometimes not be difficult to mistake the general appearance for that of Addison's disease if the history of the skin trouble were concealed.

#### *Pathology.*

The direct relationship of the disease to pregnancy is very remarkable. It seems to be the only point distinguishing it from dermatitis herpetiformis. I should like in this connexion to say a few words about eosinophilia.

#### *Eosinophilia.*

It is often stated in a general way that eosinophilia occurs in a large number of skin diseases. To test this I have made differential leucocyte counts in a number of all kinds of eruptions, and in the great majority of the commoner varieties there is no eosinophilia at all.<sup>1</sup> If it be granted that nothing less than 5 per cent. of coarsely granular eosinophile cells in the blood can be termed eosinophilia, it is quite exceptional for cases of eczema, psoriasis, and the like to exhibit it. The reverse is true of the bullous dermatoses, however. There are, of course, a good many cases of pemphigus in which no eosinophilia is found at a single examination, and the percentage of coarsely granular eosinophile corpuscles varies not only in different individuals suffering from the same disease but also in the same individuals at different times. Nevertheless, in patients suffering from pemphigus or from dermatitis herpetiformis, eosinophilia is the rule rather than the exception, as Bettmann-Darier, and others have pointed out. The degree of eosinophilia in the blood is moderate rather than great, the coarsely granular eosinophile corpuscles numbering something between 5 per cent. and 15 per cent. of all the leucocytes in typical cases.

It is worthy of note that the eosinophilia is not in the blood alone, but that the eosinophile corpuscles are also present in the inter-epithelial lymphatic spaces, where they may be seen in the microscopical sections of the skin; and, further, that in the fluid of the blebs themselves there are leucocytes, of which over 70 per cent. may be of the eosinophile variety. It is recorded as a curious fact that, although the fluid in the natural blebs contains



so large a preponderance of eosinophile cells, there is no such preponderance of these corpuscles in the fluid of an artificial blister made upon the patient's skin, by cantharides, for example.

Herpes gestationis agrees with the other bullous dermatoses in exhibiting eosinophilia. The differential leucocyte count in the case mentioned above was as follows: Small lymphocytes, 11 per cent.; large hyaline lymphocytes, 4 per cent.; polymorphonuclear cells, 71 per cent.; and coarsely granular eosinophile cells, 14 per cent. The significance of the eosinophilia is obscure. There are, of course, three main groups of conditions in which eosinophilia occurs. These are: First, those parasitic affections in which there is constitutional disturbance, notably in patients suffering from *Ankylostomum duodenale*, *Trichina spiralis*, *Filaria sanguinis hominis*, *Bilharzia haematobia*, hydatids, and sometimes with taeniae and scabies, but not with the milder parasitic affections such as those of *Trichocephalus dispar*, *Oxyuris vermicularis*, *Ascaris lumbricoides*, or *Tinea tonsurans*, and allied trichophytic affections. Secondly, true spasmodic asthma, in which eosinophilia is found during the attacks but not between them. Thirdly, certain skin diseases, chiefly the bullous dermatoses, as mentioned above. It is difficult to say why eosinophilia should be a prominent feature in these three groups of conditions and not in a great many other affections. It is thought that a poison of some kind is at the bottom of it in the parasitic diseases; that a toxin can produce a local eosinophilia was shown in the Johns Hopkins Hospital, where the vascular spaces around appendicular abscesses were demonstrated to be full of eosinophile corpuscles, although there was no excess of eosinophile cells in the general circulation. True asthma, however, is usually regarded as primarily a nervous phenomenon, and it is not at all clear why it should be associated with eosinophilia. It may be that there is an unknown poison which starts the neuro-muscular spasm in the bronchioles; otherwise it would seem that eosinophilia may have a nervous as well as a toxic origin.

The eosinophilia of skin diseases has been so little studied that it does not seem to be known whether the blood contains the excess of eosinophile cells before the eruption comes out, or whether the bullae always precede the eosinophilia. If the former were the case, then both the eosinophilia and the vesicles would probably have a common cause, whether that were nervous or toxic. The general opinion is, however, that the eosinophilia is the result of the skin lesion, due, perhaps, to the absorption of something from the skin in a way that would be comparable to the eosinophilia of ankylostomiasis, where there is supposed to be absorption of some toxin from the bowel. This raises the question of the pathology of the bullous dermatoses in general and of herpes gestationis in particular. It seems fairly clear that their causes arise within the body, and that the lesions are not due to agents acting directly upon the skin from without. Bac-



teriological investigations have proved negative, the only micro-organisms that have been cultivated from the blebs being such as are readily explained as derived from accidental contamination from the skin.

### *Histology.*

The actual process by which the vesicle or bulla develops seems to be as follows. There is a local dilatation of the papillary and subpapillary blood vessels, and an almost simultaneous increase in the quantity of lymph in the spaces around the prickle cells of the epidermis. The local erythema is caused by the vascular dilatation and the itching is doubtless due to the tension put upon the cutaneous nerve endings by the sudden increase in the quantity of pericellular lymph. There is no proliferation of the cells themselves, such as occurs in eczema, though leucocytes may accumulate in the part by diapedesis. The pericellular lymph goes on increasing in quantity until the protoplasmic bridges between the prickle cells are mechanically torn asunder; larger and larger numbers of dilated intercellular spaces in this way become united into a single cavity and a vesicle results. If the lymphatic dilatation is spread uniformly over a comparatively wide area, a single large bulla is formed; if within the same area the dilatation is irregularly distributed with several maximum points, a group of smaller vesicles is produced; if the original area of vascular dilatation is small, a single vesicle, too small to be termed a bulla, results. The size of the bleb is therefore to some extent an accident. The depth at which the vesicles form is also more or less accidental; in some cases the fluid accumulates quite close beneath the stratum corneum; in others, so deeply that only the papillary layer separates it from the corium. The transitional layer is the level at which the lymph is able to separate the cells with greatest ease, so that it is here that the vesicle or bulla originates most commonly. The surrounding prickle cells swell up, become more or less spherical, and assume an appearance which led Professor Unna to term them "balloon cells." Notwithstanding their altered appearance, they still retain their nuclei and their vitality for a long while, though many of them ultimately become more and more swollen and homogeneous, and finally break up.

### *Allied Conditions.\**

It would not, I think, be surprising if the degree of lymph accumulation between the prickle cells sometimes stopped short of vesicle formation. Local patches of erythema, accompanied by much itching and even pain, would then be the only features of the

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\* See also H. Radcliffe Crocker, Lettsomian lectures upon the Conditions which Modify the Characters of Inflammations of the Skin and their Influence on Treatment, Lecture II, the *Lancet*, March 7th, 1903, p. 643.

disease, and, as Sir Cooper Perry has pointed out to me, there are not a few cases in which women during each successive pregnancy suffer from skin trouble of this kind. The characters of the lesion are then such as lead to a diagnosis of pruritus or urticaria, as the case may be. The relationship between urticaria and vesicular or bullous eruptions is well seen in young children. Infants have so tender a skin that ordinary urticaria in them not infrequently ends in the production of vesicles. Some of the cases of pruritus or urticaria of pregnancy are very probably examples of abortive or incomplete herpes gestationis. It would be very interesting to know whether or not there is eosinophilia in these patients too, but I have not yet been able to make any investigations upon this point.

The changes described above suggest that the trouble arises from there being something the matter within the vessels themselves. It would seem that the mischief is either primarily nervous or else that there is some poison circulating within the vessels at the time. The generally accepted view appears to be that the disease is primarily nervous, in which case it would be analogous to herpes zoster, or more correctly perhaps with factitious urticaria, or with angioneurotic oedema. On the other hand, by analogy with the urticaria which sometimes follows the ingestion of certain foods, or with the vesicular or pustular eruptions that may follow the administration of certain drugs, such as the bromide or the iodide of potassium, it is at least quite as likely that there is a toxic agent or poison concerned in herpes gestationis. If the disease were purely the result of an angioneurosis it would seem surprising that the eruption should so often be restricted entirely to the times of pregnancy. It is true that cases have been recorded in which the attacks came on apart from, as well as during, pregnancy, but this is distinctly unusual, and such cases would be termed true dermatitis herpetiformis rather than the distinct variety we are now speaking of. Pregnancy seems to be an essential cause of the latter. The patients are not necessarily of nervous disposition; the lady whose case has been given above was a most sensible woman; there was no history of nervous disorder in her family, nor of nervous shock nor of anything of that kind in herself. Moreover, one cannot trace any hereditary tendency to the disease, such as is well known in cases of angioneurotic oedema. It is not at present possible to bring forward any conclusive arguments, however, one way or the other as to whether herpes gestationis is primarily nervous or primarily toxic in origin. No toxin is known, but this does not prove that none is present. It is even possible that no abnormal substance is present in these cases at all, but that the patients are unduly susceptible to some compound which is a normal metabolic product of the pregnant state. The idiosyncrasy of some persons in regard to strawberries might be used as a comparison. Most people can partake of this fruit in moderation with impunity, but a few

cannot eat a single strawberry without suffering acutely from urticaria.

The pregnancy itself is not interfered with by the skin disease provided that suitable treatment is adopted to prevent pyodermla and to enable the patient to get a sufficiency of sleep. The children are born living and healthy, and it seems that the offspring of a mother who has been subject to the complaint are not particularly liable to any of the bullous dermatoses, nor are the females more liable than others to herpes gestationis. It is, however, very difficult to obtain direct evidence on this point, because few physicians see any large number of the cases, and fewer still are likely to pay particular attention to the point in question.

This may, perhaps, be a good opportunity for mentioning a subject which Dr. Lauriston E. Shaw has spoken to me about sometimes—namely, that of the necessity for collective investigations being made upon special clinical and pathological points of this kind. There are many questions which, owing to the smallness of the number of cases that any individual is likely to see, can only be elucidated by collective inquiry. The Clinical Society, the Royal Medical and Chirurgical Society, and other similar bodies have from time to time instituted inquiries of the kind, but for the most part the data have been collected *after* the cases have been seen—from ward reports, *post-mortem* records, and so forth. The very points upon which one wishes information are often not referred to at all in these, simply because the student or other person who wrote the report had not the knowledge or the interest to make a note about it. There are many conditions in which those who, having made a study of the cases up to a certain point, and having come across difficulties upon which they can nowhere find fuller information, could advise others as to special points to be upon the watch for and to pay particular attention to in *future* cases as they come under observation. The selection of the questions that might seem suitable for collective investigation in this way must necessarily lie with those who already know much. Dr. Mahomed when he was alive initiated a system of the kind, but it died with him. The anatomists have a list of points upon which collective investigation is required, and in the dissecting room at Oxford there was a book in which were entered certain features of the anatomy of the vermiform appendix in each cadaver that was dissected, in order that by the accumulation of these and of a similar series of records from various other dissecting rooms certain debated points as to this particular part of anatomy might finally be settled. Some similar scheme might be possible as an assistance in settling debated points in medicine a few at a time. It would require a central authority for the selection of the points to be investigated, and the collaboration of all physicians at all hospitals would need to be sought. The central authority would doubtless be a permanent committee of physicians, and if the scheme were



feasible at all the selection of such a committee for the direction of collective inquiry into obscure or debatable points in medicine and pathology would best, perhaps, be made under the auspices of either the Association of Physicians of Great Britain and Ireland or else of the Royal Society of Medicine of London. If Dr. Shaw's suggestion commends itself to others it should not be a difficult matter for a beginning to be made.

One might be asked, for example, whether an unmarried lady who had suffered from severe dermatitis herpetiformis previously to marriage would be likely to have still worse attacks of this disease should she marry and become pregnant. There are, so far as can be ascertained, no statistics to help one to answer such a query, important though it might be in some particular case. The general impression that is left upon one's mind after seeing a few cases and reading of as many more as one can find is that dermatitis herpetiformis and herpes gestationis, though in many respects so similar to one another, are yet sufficiently different to warrant the statement that pregnancy is by no means likely to bring on an attack of the former, though almost certain to cause a repetition of the latter. Again, one might be asked whether a patient who has suffered from dermatitis herpetiformis before marriage or from herpes gestationis after marriage would be likely to transmit the tendency to either disease to her children. As has been mentioned, one's general impression is that there is no likelihood whatever of such transmission, but it would be much more satisfactory if there were clear facts to base such an opinion upon, and such facts could best be accumulated by a collective inquiry.

#### OTHER SKIN DISEASES IN RELATION TO PREGNANCY.— IMPETIGO HERPETIFORMIS.

It has been suggested above that the pruritus, erythema, abnormal pigmentation, and urticaria which may develop during pregnancy may be regarded as minor manifestations of that which, in its full development, is herpes gestationis. There is another skin lesion known as impetigo herpetiformis, which may, perhaps, be regarded as coming at the opposite extreme of the same series; that is to say, it seems to be a virulent degree of herpes gestationis, dangerous to life. Fortunately, the disease is very rare, and a short account of it will suffice. According to Dr. J. F. Payne,<sup>2</sup> the majority of the cases have been met with on the Continent, and all but two of them have been in pregnant women. The eruption is not vesicular but pustular, groups of small pustules upon a red swollen base from  $\frac{1}{2}$  in. to 1 in. in diameter appearing first in the groins, armpits, and mammary regions, and thence spreading until the whole of the body may be covered. The pustules dry up with the formation of scabby crusts, fresh pustules appear in the adjacent skin, and so on, the process extending in a circinate



manner. No ulceration results, but there is severe constitutional disturbance. The patient has continuous fever of the remittent type, and with each new crop of the eruption there may be an exacerbation of the pyrexia with occasional rigors. Vomiting and delirium are usual, and the patient nearly always dies within a few months. Parturition does not prevent the fatal termination. Cases of recovery from one attack have been recorded in which a succeeding pregnancy led to a return of the impetigo herpetiformis with fatal result.

The *post-mortem* examinations have shown no evidence of pyaemic or septicaemic infection. The general opinion appears to be that both the skin trouble and the constitutional disturbances are the result of an internal toxæmia, and it seems reasonable to suppose that a similar toxæmia rather than a primarily nervous cause is at the root of the whole series of lesions that have been mentioned, from apparently simple pruritus at the one end of the chain to herpes gestationis and to impetigo herpetiformis at the other.

There are only two other skin diseases upon which pregnancy seems to exert any definite influence. These are eczema and psoriasis, and it is only upon the latter that the effect of pregnancy is at all marked.

#### ECZEMA AND PREGNANCY.

Eczema is so very erratic in its behaviour that it is always very difficult to attribute any exacerbation in it to any particular cause. It is true that certain women, who never suffer from eczema otherwise, may develop a skin eruption which is apparently an eczema during pregnancy. The skin lesion may be papular or it may be vesicular—eczema papulosum or eczema madidans as the case may be; but when it occurs only during pregnancy and not between whiles it may be suggested that it is really allied to the urticaria and to the herpes gestationis that we have been discussing rather than to true eczema. The matter could be decided by microscopical examination of sections of the skin to determine whether there was epithelial cell proliferation, as in eczema, or none, as in herpes gestationis, but no histological work appears to have been done upon this particular point, and I have had no opportunity of doing any myself. When, on the other hand, a lady is subject to undoubted attacks of eczema apart from pregnancy, it by no means follows that the skin trouble will become worse during the pregnant state; if any general rule can be laid down it would be that the patient's eczema will very likely be mitigated rather than made worse during pregnancy.

#### PSORIASIS.

Psoriasis is more definite in its behaviour during and after pregnancy. Before the birth of the child the mother, if she be already subject to psoriasis, will either be very

much less troubled with it than before, or else will develop a severe exacerbation. It is not possible to give any certain prognosis as to which of these two things will occur, but more patients have their skin disease mitigated than increased whilst they are actually pregnant. On the other hand, the effect of lactation upon psoriasis is almost invariably bad. The eruption is liable to increase during the puerperium in any case, but if the mother suckles her child she is almost certain to develop a very severe attack of the psoriasis. This, therefore, is one of the conditions under which the mother ought not to suckle her child. Artificial feeding of the infant should be adopted from the beginning and immediate steps be taken to dry the mother's breasts.

#### THE PYELONEPHRITIS OF PREGNANCY.

Leaving the skin diseases now, we may pass on to the discussion of a condition in which, although the pathology is of quite a different kind, pregnancy again appears to be an important factor in the causation of the trouble. This is the pyelonephritis which of late years has been recognized with increasing frequency in pregnant women. Mr. G. Bellingham Smith has recorded several cases in the *Journal of Obstetrics and Gynaecology* (1905) and others in the Guy's Hospital Reports (vol. lx, 1906); upon the Continent and in the English journals there have been a good many papers upon the subject during the last few years, such as those of Reblaub, Jeannin and Cathala, Vinay, Cumston, and others. The observations made previously to 1899 were summarized by Cade in *L'Obstétrique* (vol. iv, 1899, p. 230).

#### *Illustrative Cases.*

The following are notes of two cases that have recently been in the medical wards at Guy's Hospital, the one under myself, the other under Dr. A. F. Hertz in the first instance and under Dr. G. Newton Pitt subsequently. These two examples are chosen, not only because they were in the wards almost at the same time, but also because they exemplify two very different degrees of the severity of the disease.

#### CASE I.

The patient, aged 28 years, had had two children, now aged 5 and 2 years respectively; she had had no miscarriage and she was pregnant for the third time when, at the beginning of the fifth month, she was suddenly seized with severe pains round the waist. The suddenness of the onset of the symptoms may be gathered from the fact that she was in her usual health, preparing her husband's midday dinner, when the pain seized her acutely in the loins; she was unable to go on with the dinner preparations; she took to her bed and remained there a fortnight under treatment before she was transferred to the hospital. The pains across the loins persisted all the time, waxing and waning to some extent, but not in such a way as to suggest colic. Vomiting had been frequent, especially after food, and this notwithstanding her diet being milk and soda-

water only. In addition to the vomiting there had been severe headaches and upon several occasions rigors. The skin was dry for the first five days but since then there had been copious perspirations.

Upon examination the chief abnormality was in connexion with the right kidney. The abdomen was supple, and it moved well with respiration. The kidney could not be palpated, but there was a slight degree of fullness in the right flank, and at a spot just below the right twelfth rib there was acute tenderness on the slightest pressure. The bladder was normal, and there was no frequency of micturition. The urine was alkaline, abundant, and of specific gravity 1010; it contained enough albumen to give a marked cloud with the boiling test, and microscopically there were large numbers of pus corpuscles, a few renal cells, and an occasional granular tube cast. A catheter specimen of the urine, examined bacteriologically, gave a pure culture of *Bacillus coli communis*. There had been considerable pyrexia during the fortnight previously to admission. Here is the temperature chart for the first two weeks after admission:

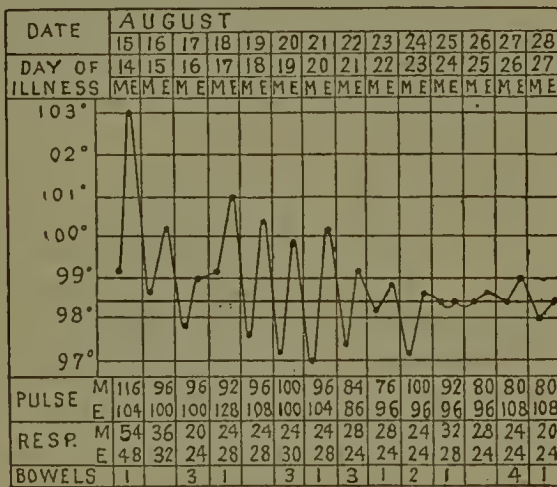


Chart 1.

Absolute rest in bed and the administration of urotropine were followed by rapid alleviation in the symptoms, and the patient went out in three weeks' time, feeling quite well, though there were still a few pus corpuscles in the urine. It was by her own desire that she went out, and it would certainly be wiser in other similar cases to continue the treatment till term; for within a fortnight she had all her acute symptoms back again, and she had to be put back to bed. Fortunately, the severer symptoms of the relapse passed off in a similar way to those of the original attack, but the patient had to be extremely careful for the rest of her time. Her baby was born alive at full term. The puerperium was normal, and the patient is now strong and well. Her urine has been quite free from pus and from other abnormal constituents since that time.

The above might be termed an ordinary case of the kind; the following is an instance of a much more severe type:

#### CASE II.

The patient, aged 24 years, had been married two years, and had had no living child, though nearly a year ago she had a



miscarriage at the fourth month, followed by rapid and uninterrupted recovery. She was now five and a half months pregnant. She had been perfectly well until a fortnight previously to admission, when, without apparent cause, she suddenly experienced severe pain in the right loin, which persisted and soon extended round from the loin into the right iliac fossa. She had always been subject to constipation, her bowels being moved only twice a week as a rule, and during the fortnight previously to her admission to hospital enemata had been required upon several occasions. Vomiting had occurred only once. The patient's temperature was 103.6° F, her pulse-rate 124, and her respiration-rate 26 per minute. The uterus extended to just above the umbilicus, and, owing to the pregnancy, palpation of the rest of the abdomen was difficult. Tenderness was more marked in the right iliac fossa than elsewhere, and there was also cutaneous hyperaesthesia here. The general impression at first sight was that the patient had appendicitis, but more detailed examination showed that the tenderness extended from the right iliac fossa well back into the right loin and as high as the twelfth right rib. There was only slight rigidity of the muscles over the right iliac fossa. If the condition were appendicular the same symptoms might have been caused if the inflammatory trouble had tracked up behind the ascending colon into the perinephric tissue, but the patient herself was quite clear that the pain had started in the right loin and had thence extended into the right iliac fossa, and not vice versa, as would most likely have been the case if the trouble had been primarily appendicular. There was no lump to be felt and the right loin was not filled out. The urine was acid, of a specific gravity 1020, and a pale yellow colour. It contained a flocculent deposit of pus, a fair quantity of albumen, and no obvious blood. Microscopically pus cells without crystals abounded in the deposit, and there were also many renal cells, both from the pelvis and from the tubules, a few red blood corpuscles, and several tube casts, chiefly of the granular variety. The other general systems were natural, except that the vesicular murmur was deficient at the base of the right lung. A diagnosis of pyelonephritis of pregnancy was made.

One point of particular interest was that the patient's leucocytes were increased up to 25,000 per cubic millimetre of blood, so that a leucocyte count is apparently of no service in helping to distinguish this disease from appendicular abscess and the like, though it helps in excluding typhoid fever—a condition which the pyrexia might suggest. The accompanying temperature chart sufficiently indicates how ill the patient was.

A catheter specimen of the urine, examined bacteriologically, gave a pure culture of *Bacillus coli communis*, and a similar result was obtained upon three subsequent examinations. The vagina and uterus were perfectly healthy, and there was no disease of the bladder. The latter was examined with the cystoscope and purulent urine was seen issuing chiefly from the right ureter, but the mucosa of the bladder itself was perfectly normal. There was no dilatation of the vesical orifices of the ureters. The pain in the right loin, with exacerbations accompanied by vomiting, persisted in spite of everything that was done. The pyuria and albuminuria showed no abatement, and a moderate degree of jaundice developed. The patient seemed to be getting steadily worse, and at the end of the sixth week she consented to undergo an operation with a view to deciding whether there was anything in the right renal region that could be either removed or drained. Mr. F. J. Steward exposed the kidney and found that it was studded all over with small abscesses. There was no large collection of pus that could be incised and drained, and







the patient's condition was so critical—her pulse-rate being over 170—that nephrectomy was out of the question, so the wound was sewn up, a space being left for a gauze drain. The ureter had been felt to be dilated above the bladder, although it had been shown by the cystoscope that the vesical orifice was normal.

The patient steadily improved after the operation, notwithstanding the fact that nothing particular was done. It should be noted that no pus and no urins drained through the lumbar wound for a fortnight after the operation, but that upon the fourteenth day urine came away from it in abundance, and continued to do so for some weeks after the patient was convalescent. It is very difficult indeed to say what part the operation itself played in the subsequent recovery, particularly in view of the vaccine treatment that was adopted about the same time. The vaccine was prepared from cultures of *Bacillus coli communis* obtained from the patient's urine. The injections were made at intervals of about a fortnight, as shown upon the temperature chart, and each dose consisted of the products of 500,000,000 bacilli. To judge by the chart the improvement dated from the exploratory operation itself; it was already well marked before urine began to come through the loin, so that actual external drainage of the abscesses in the kidney did not seem to be the deciding factor in the case. The urine continued purulent; indeed, the quantity of pus in the urine was noted as being greater after the operation than it was before it. It is possible that in some way the manipulations which were necessary at the time relieved some pressure that had previously existed upon the right ureter in its pelvic course, and that the discharge of urine from the wound in the loin fourteen days after the operation was a sign that the obstruction to the ureter had then re-established itself. In any case, the patient steadily improved, although pyuria persisted. It was not until the temperature had already been normal for several days that the pregnancy showed any signs of terminating. Without much warning and without difficulty a living premature child was born on the seventy-seventh day of the illness. The puerperium was uneventful. The pus and albumen had both entirely disappeared from the urine within a month of the birth of the child. The wound in the loin had healed up, and the patient was soon up and walking about, quite well.

Before passing on to discuss the pathology of the malady in general, stress may perhaps be laid upon three particular points in the above case. The first of these is the dilatation of the ureter that was demonstrated—a dilatation not beginning at the bladder itself, but just above the bladder about the level of the pelvic brim. The second is the fact that the inflammation is not confined to the pelvis of the kidney in these cases, but extends right up into the cortex, as was demonstrated at the operation. And the third is that, notwithstanding the existence of large numbers of small abscesses in a kidney affected by an extreme degree of suppurative pyelonephritis of this kind, uraemia in the ordinary sense need not supervene and the patient may recover completely. No doubt it depends to some extent upon the nature of the organism present whether recovery is likely to occur or not, and in these cases it is always, or nearly always, the *Bacillus coli communis*. This organism, however, is usually accredited with particular virulence when it affects parts outside the

allimentary canal; and if the miliary abscesses had not been ocularly demonstrated at the operation it would have been difficult, in view of the subsequent complete recovery, to have believed that such abscesses had actually been present. One wonders whether it is as true as it is usually held to be that multiple abscesses in another organ—namely, the liver in suppurative pylephlebitis—must necessarily be fatal also. In view of these multiple abscesses in the kidney getting well it would seem possible, if not probable, that similar multiple abscesses in the liver may get well too sometimes.

### *Pathology.*

Turning now to the pathology of the pyelonephritis of pregnancy, there are certain points that are fairly clear. The cases that have been collected by Mr. Bellingham Smith and others all indicate that previous to the pregnancy there was no renal trouble. It is probable, therefore, that the gravid uterus is a responsible factor in the production of the mischief. It is also clear that the pyelonephritis is not secondary to cystitis, for in practically all the patients the bladder has been healthy—at any rate, at the beginning of the disease. Further, it has been demonstrated at the necropsy in some cases, and at operation in others, that there is dilatation of the ureter beginning about an inch above the bladder. Putting all these facts together, it seems almost certain that the sequence of events is: Enlargement of the uterus; compression of the ureter against the brim of the true pelvis; consequent difficulty in the ejection of urine secreted by the corresponding kidney; infection of the urine retained in the partially obstructed ureter and renal pelvis; and subsequent spread to the kidney substance itself. The pyelonephritis of pregnancy would thus be comparable in some respects with pyelonephritis due to other causes, such as enlargement of the prostate in man; and just as in the latter case removal of the obstruction tends to cure the renal mischief, so does the birth of the child result in most cases in rapid amelioration and even complete cure of the trouble from which the pregnant woman has suffered.

It is a curious but very definite fact that in nearly every case the right kidney is very much more affected than is the left. In both the patients of whom notes have been given this was so. It is probable that the left kidney does not escape entirely; and, indeed, there is usually some pain in the left loin as well as in the right, but in the majority of cases the symptoms indicate that the mischief is mainly on the right side. There have been several explanations offered to account for this; perhaps the best is that of Cumston. He states that whilst the pregnant uterus develops its borders come nearer to the ureters, upon which they become pressed. The uterus develops much more to the right than to the left; it also inclines to the right, and besides this it undergoes a



rotation on its vertical axis, and turns in the direction of its greatest development—that is to say, to the right, thus freeing the organs on the left side, and exerting a greater compression on those of the right. Be this as it may, the facts that the ureteral obstruction begins at the level of the pelvic balm, that it is in some way due to the pregnant uterus, and that the right ureter is, as a rule, more obstructed than is the left, have been repeatedly demonstrated.

Seeing that partial stenosis of the ureter by the pregnant uterus is generally regarded as the essential predisposing factor to this kind of pyelonephritis, it might very well be suggested upon theoretical grounds that the illness ought to be much more common and much more serious in those who have deformed and particularly contracted pelvis and in those who have pelvic tumours, such as uterine fibromyomata or ovarian cysts, in addition to their pregnancy. These complications have existed in a few of the cases, and theoretically they should play an important part in the pathology of the condition. Nevertheless the existence of pelvic tumours or the like with pregnancy is by no means essential, or even common, as a cause of the pyelonephritis. The cases recorded have almost all had normal pelvis and normal pelvic organs. The disease is therefore one which may arise in otherwise healthy women.

In regard to the question of whether a woman is liable to it during her first or a later pregnancy, opinions differ. It seems quite clear that the first few pregnancies may be quite uncomplicated and yet that pyelonephritis may develop during a later one; several observers lay stress upon its occurrence in primiparae, but the truth seems to be that it may arise during any pregnancy, and that in the differential diagnosis no stress can be laid upon the fact of the patient being a primipara or otherwise. It is clear that if obstruction to a ureter is an essential factor in the disease, the trouble is not to be expected in the earliest months of pregnancy. This is borne out by the cases themselves. The pyelonephritis may not appear until quite late in the pregnancy, but in the typical cases the mischief begins about the fifth month, as in the two cases described above.

### *Bacteriology.*

The bacteriology of the condition is very constant. In all but a very few of the recorded cases the organism that appears in cultivations from the purulent urine has been the *Bacillus coli communis*. It has nearly always been in pure culture. Mr. Bellingham Smith found it in seven consecutive cases, and in only one case, recorded by Vinay, was the mischief attributable to another micro-organism—namely, a streptococcus.

There is some difficulty in determining the route of infection; this applies, of course, not only to the pyelonephritis of pregnancy, but also to the similar suppurative lesions that may ensue when there has been residual urine

in the bladder for a long time, even though no catheter or other similar instrument has ever been passed. The three paths by which the micro-organism might, it may be supposed, reach the kidney are: first, from the bladder, ascending by the ureters; secondly, by the lymphatic vessels; or, thirdly, by the blood stream. It must to some extent remain a matter of opinion as to which of these three paths is the more usual in these cases. Personally I agree with Mr. Bellingham Smith in thinking the blood stream the more likely route of infection, his arguments being as follows: Whereas it is true that, as Opitz urges, the female urethra always contains organisms and that the bladder in pregnancy is very liable to cystitis, nevertheless there are two objections to the view that the path of infection in the pyelonephritis of pregnancy is via the bladder—one anatomical, the other clinical. The anatomical objection is that the ureter in these cases is dilated, not in its whole extent, but only above the brim of the pelvis; the valve-like opening of the ureter into the bladder, which normally protects the former from infection, is still present and in perfect working order; there is no dilatation of the vesical end of the ureter, such as to cause a free communication between the latter and the bladder, and consequently there is no free path for the ascent of organisms from the bladder into the ureter. The clinical objection is still greater. The chief feature of pyelonephritis in pregnancy is the presence of pus in the urine without any symptom pointing to cystitis. None of the cases under discussion have afforded any evidence of preceding cystitis, and cystoscopic examination in the severer of the two cases of which notes have been given showed that the bladder was perfectly healthy. There are no doubt other cases of pyelonephritis secondary to existing cystitis, the symptoms being aggravated by the existence of pregnancy, and in such cases the path of infection would doubtless be from the bladder, just as it might be in a non-pregnant person; but in the cases of pyelonephritis under discussion there is no cystitis, pregnancy is an essential factor in the disease, and it seems unlikely that the organisms reach the kidney by ascent from the bladder.

Infection by the lymphatic vessels is very difficult either to prove or to disprove, and there is little or nothing that can be stated definitely about it. Infection by the blood stream, on the other hand, is possible, and, if the vesical and lymphatic routes can be excluded, even probable. Experiments have been made on animals in which, after artificial stenosis of a ureter, purulent nephritis followed injection of *Bacillus coli communis* cultures into the blood stream. Moreover, it has been shown that the healthy kidney sometimes excretes micro-organisms such as tubercle bacilli and typhoid bacilli in patients and animals who are suffering from an apparently local tuberculosis or from apparently uncomplicated typhoid fever. In these cases the micro-

organisms have presumably reached the kidney in the blood stream, and if tubercle and typhoid bacilli can do so it would not be surprising if the *Bacillus coli communis* did so too. The healthy kidney would eliminate the bacillus without itself suffering. The existence of stenosis of the ureter might well cause the urine containing such bacilli to stagnate long enough to allow of infection of the walls of the passages, even without supposing that there was diminished resisting power in the parts owing to the obstructed outflow. The ease with which the *Bacillus coli communis* can reach the blood stream is well known from *post-mortem* examinations, where cultivations from organs situated far from the bowel nearly always yield this micro-organism in cultures made soon after death. It is held by some that a similar escape of the *Bacillus coli communis* from the bowel into the blood stream can occur during life, particularly when there are abnormalities in the functions of the alimentary canal.

This raises the question of whether the pyelonephritis of pregnancy can occur when there has been no abnormality in the intestinal functions, or whether, in addition to pregnancy and partial stenosis of the ureter, some error of the bowels, particularly constipation, is essential to its production. This is a very difficult matter to decide. It is very certain that a great many pregnant women may suffer from constipation without any other deleterious effects. Nevertheless, granted that a patient were on the verge of developing pyelonephritis, the existence of severe constipation might very possibly cause a certain number of colon bacilli to enter the blood stream and thus prove to be the final or determining factor in the illness. This seems to have been the case, for example, in connexion with the second patient described above; always very costive, she was suffering so much from constipation just before the pyelonephritis set in that she could only get her bowels to act by the use of repeated enemata.

### *Effect upon the Pregnancy.*

A number of questions arise, to each of which the physician may be required to give an answer if he can. Amongst these are the following: To what extent does the pyelonephritis interfere with the course of the pregnancy? Is it likely that the child will be born dead? Seeing that pregnancy is a fundamental factor in the pyelonephritis, ought obstetrical measures for the termination of the pregnancy to be advised? Is the time of labour one of special danger? Is the patient particularly liable to uraemic symptoms? Is there any relationship between pyelonephritis and puerperal eclampsia? Is the condition likely to be completely cured after labour, or is a residuum of kidney inflammation to be expected? Is the patient very liable to have a recurrence of the pyelonephritis in a succeeding pregnancy?



It is only by a collective inquiry, in which mild as well as severe cases are included, that conclusive answers can be given to these questions. Under present conditions it is dangerous to base opinions upon published cases only, because those which are thought worthy of being published are often not the ordinary cases, but rather those which present points of special interest. On the other hand, an individual can scarcely hope to meet with a very large number of cases himself, so that until records of consecutive and unselected cases can by some means be gathered together it is only possible to base one's opinion either upon recorded, and therefore selected, cases, or else upon the few cases that one has oneself watched.

It would seem that, diagnosed early and treated by confinement to bed with antipyuric remedies, the condition usually tends towards resolution, notwithstanding continuance of the pregnancy. Moreover, in the majority of what may be called cases of ordinary severity the pregnancy is not particularly apt to come to an end prematurely. The children do not show any special liability to die *in utero*, and the mother is not subject to uraemic convulsions at the time of labour. No doubt there are individual cases in which the illness is so severe that it might be wise to advise relief to the ureteral obstruction by the use of obstetric measures for emptying the uterus. The kind of case in which this might be the best course to follow would probably be one in which the renal mischief had set in with severity during the earlier months of the pregnancy and had then persisted for a month or more without abatement in the symptoms, notwithstanding all the medicinal treatment available. Such cases as these are distinctly the exception, however. The majority of the patients require the adoption of no obstetrical measures for the time being. Treatment upon purely medical lines—by absolute rest in bed, light nourishing diet, laxatives, and such drugs as are known to benefit pyuria, begun early and carefully followed, will usually relieve the patient of her untoward symptoms comparatively soon—that is to say, within three weeks or a month. The pyuria will often persist for a month or six weeks after the patient herself feels quite well, and, unless considerable care is observed, a relapse is apt to occur before the pregnancy reaches term. Repeated microscopical examination of the urine is therefore essential, and medical supervision is required as long as any pus is present. Eclampsia is not to be expected, and the patients nearly always get perfectly well of their pyuria after the child has been born.

It would not be at all surprising if similar pyelonephritis were to recur in succeeding pregnancies, and cases are on record where this has actually been the case. This is not the invariable rule, however. If the pyuria is completely cured after one pregnancy, and care is subsequently taken to ensure that there is neither constipation nor diarrhoea such as might predispose to invasion of the body by the *Bacillus coli communis* from the intestines, it



is quite possible for a succeeding pregnancy to pass by without any symptom of pyelonephritis at all.

In conclusion of this lecture stress may well be laid upon the fact that the pyelonephritis of pregnancy may easily be mistaken for something else. The milder cases may be regarded as simple pain in the back, as lumbago, as influenza, and so forth; severer cases may be thought to have pneumonia, pleurisy, or the like; the most severe cases may be diagnosed as appendicitis or as some other intra-abdominal condition. The main symptoms of the disease are backache and pyrexia, with or without headache, vomiting or rigors, and unless the urine is carefully examined for pus corpuscles the real cause of the trouble might readily be overlooked.

#### REFERENCES.

<sup>1</sup> Herbert French: Eosinophilia in Skin Diseases, Guy's Hospital Reports, 1903. <sup>2</sup> Clifford Allbutt: *System of Medicine*.

## LECTURE II.

OTHER SUPPURATIVE RENAL AFFECTIONS IN RELATION TO  
PREGNANCY: TUBERCULOUS AND CALCULOUS DISEASES.

MR. PRESIDENT AND GENTLEMEN,—The pyelonephritis which pregnancy itself gives rise to having been discussed, there remain two other suppurative renal affections to be mentioned. These are the various degrees of kidney mischief that may be due to stone and to tuberculosis respectively. There is little evidence to show that pregnancy is itself liable to give rise to either of these, and in the case of a tuberculous kidney the patient is, as a rule, so invalided that pregnancy is but rarely to be found associated with it. There has been no case of pregnancy coincident with tuberculous kidney in Guy's Hospital in the last twenty years. With renal calculus, on the other hand, the symptoms may be in abeyance for longer or shorter periods, and the patient is not necessarily such an invalid that pregnancy may not occur. The question will then arise as to what the effect upon the kidney is likely to be in such a case. It is clear that if a previously healthy woman may develop pyelonephritis during pregnancy, as described in the previous lecture, a woman who already has a lesion which also predisposes to pyuria must be in a position of increased danger when pregnancy occurs. On the other hand, the degree to which the kidney, or kidneys, may be already damaged by the calculi is so extremely variable that it is almost impossible to say what is going to happen when such a case comes under observation. If the calculus is a small one confined to the renal pelvis, the general substance of the kidney being but little affected, it is quite possible for the pregnancy to run its course without any trouble arising from it at all. If the stones are confined to one kidney and have led to its conversion into a hydronephrotic bag, the other kidney may have hypertrophied by way of compensation, and the effect of pregnancy will be similar to that in cases where, after operation, only one kidney is left—a point to be mentioned again below.

Colic and haematuria may occur in either of these cases, just as they may in non-pregnant persons. Treatment should then be directed to the renal condition, and the probability is that the untoward symptoms will subside and that the pregnancy will run its natural course, as was the case in six out of seven patients in the hospital. On the other hand, a patient with a renal calculus that is

already causing suppurative inflammation of the kidney is bound to be a source of grave anxiety to her medical attendant should she become pregnant, especially from the fifth month onwards, that is to say during the time when there is particular liability for the pregnancy itself to cause pyelonephritis. It is doubtless possible by keeping the patient at rest, by preventing constipation or diarrhoea, and by administering antipyretic remedies, to enable her to reach her full term of pregnancy; but there are cases in which the suppuration in the kidney will become worse, and the question will arise as to whether or not obstetric measures for terminating the pregnancy should be advised. One of the seven cases alluded to above proved fatal; it may probably be regarded as one in which pregnancy was the main cause of death by leading to a pyelonephritis upon the top of calculous disease. The following are brief details of the case:

The patient was a young woman who had had pain in her right loin, which in view of the subsequent events was doubtless due to a calculus. She was otherwise in excellent health. She married and remained well until she was five and a half months pregnant. She then began to suffer from aching pains across her loins and from repeated vomiting. There was no oedema, but the urine was found to contain 5 parts per 1,000 of albumen, with a fair number of renal tube casts, red corpuscles, and a considerable excess of leucocytes. Day by day the leucocytes in the urine became more numerous until they amounted to pus, and the quantity of pus rapidly increased until there was no doubt about there being a progressive suppurative nephritis. No tubercle bacilli were found in the deposit. The urea still amounted to 1.7 per cent., but the patient became steadily worse, vomiting on the slightest exertion and after all food. There was no pyrexia such as there nearly always is in cases of ordinary pyelonephritis of pregnancy, and there were no rigors. The bladder became infected by acute cystitis, and the question of recommending obstetric measures for emptying the uterus had arisen, when spontaneous delivery of a living female child occurred at the seventh month. The patient's general condition improved for three days afterwards, though no day passed without the occurrence of vomiting. The latter then increased in severity; drowsiness with muttering delirium and hallucinations set in, with incontinence of urine; and on the fifth day after labour the patient became comatose and died without convulsions.

At the necropsy the only abnormal organs were the kidneys and the bladder. The uterus was perfectly healthy. Both kidneys were in a state of pyonephrosis, with secondary suppurative pyelonephritis, and in the pelvis of each there were numerous irregular calculi of oxalate of lime coated with white phosphates. The ureters were but slightly dilated. The bladder was in a condition of acute cystitis without ulceration.

Apparently the sequence of events had been renal calculi, hydronephroses, pregnancy, microbial infection of the kidneys, pyonephroses, suppurative pyelonephritis, cystitis, uraemia, death. Unfortunately no exhaustive bacteriological examinations of the urine were made. One would not be surprised, in view of what has been already said in connexion with the pyelonephritis of pregnancy,

If the micro-organism had been the *Bacillus coli communis* in pure culture. This is a point for investigation in future cases.

#### NON-SUPPURATIVE RENAL AFFECTIONS IN RELATION TO PREGNANCY.

We may now pass on to consider the non-suppurative lesions of the kidney in their relation to pregnancy, and although these constitute a very big subject, and one which might easily occupy many lectures, it will be best to touch only upon a few points of it here, because there is already a great deal of literature upon the matter, much of which is easily accessible to all.

There is still a good deal of discrepancy in the views held by different observers as to the nature of the lesions in question, for whereas some pathologists describe them as inflammatory, others insist that they are not so, but are rather acute toxic degenerations of the renal cells.

*Clinical Groups.*—Clinically there are three quite distinct groups of cases which some would distinguish from one another in kind as well as in type. (1) The cases in which renal mischief of the nature of Bright's disease has been known to exist previously to pregnancy. (2) The cases in which, previously to pregnancy, the urine was perfectly healthy and no previous attack of Bright's disease had occurred; but in whom during pregnancy, and beginning, as a rule, at or before the middle of the pregnancy, puffiness of the ankles, back, and eyelids appears, the urine at the same time becoming less in quantity and containing albumen, renal tube casts, and possibly blood, in a way which closely simulates ordinary acute Bright's disease. For the sake of brevity these are referred to as the "oedema cases." (3) The cases in which the patient has seemed to be in perfect health until the later months of pregnancy, or even until immediately after labour, and then without much warning and usually with only slight evidences of oedema, develops the well known symptoms of puerperal eclampsia.

It is not at all improbable that there is a fourth clinical variety of renal disease that has a relationship to pregnancy—namely, the granular contracted kidney. It is very difficult to prove or to disprove this, because even if a granular contracted kidney in a given case owes its inception to renal trouble arising during pregnancy, the patient can still continue to live for many years without untoward symptoms, and, by the time death occurs, there will be nothing in the *post-mortem* examination to show either how long the renal mischief has been present, or how this mischief first began.

Recurrent obstruction to ureters is a potent cause of renal fibrosis, and it is conceivable that many successive pregnancies may lead to sclerosis of the kidneys without there having been any of the symptoms of acute Bright's disease. I have accumulated some evidence to show that



not only pregnancy but also pathological affections of the pelvic organs, such as prolapse of the uterus, may lead to fibrotic kidneys, with hypertrophy of the left ventricle of the heart, and all the other changes that are usually associated with red granular kidney, even including cerebral haemorrhage. The data, however, are not yet complete, so that it will be best to leave the red granular kidney out of the question now under discussion, and to confine attention to the three different clinical types of renal disease mentioned above.

First, in regard to pregnancy arising in a patient known to have Bright's disease at the time conception occurred. It is so clear that pregnancy is apt to have a deleterious effect upon the kidneys, that it is manifestly unwise for a girl or woman with existing nephritis to get married. If the urine already contains both albumen and renal tube casts, there is a great risk that pregnancy will make the condition far worse and accelerate the end. The surprising thing is that some patients known to have persistent Bright's disease before pregnancy sometimes live to bear many children, even in spite of exacerbations of their renal symptoms during pregnancy. Such cases are exceptional, no doubt, but on going through the hospital records one finds several of this kind. In one there had been all the signs of chronic tubal nephritis for thirteen years; the patient had been married for eight years, she had borne five children, and bore a sixth alive at term in the hospital. This was not a case of recurrent acute nephritis, but of persistence of both albuminuria and tube casts; it is the more remarkable in that, even without the additional strain of pregnancy, it is unusual for a patient with such a renal condition to survive so long. Such an exceptional case merely shows that both pregnancy and survival may occur in a case of chronic Bright's disease; it does not follow that medical advice should not be against marriage in other cases of the kind.

There now remain the two groups of cases in which the renal disease is directly attributable to pregnancy—namely, those who develop renal oedema in the middle months and those who develop eclampsia at the end. The fact that these two forms of renal disease are really attributable to the pregnancy is so well established that it needs no discussion. In the majority of the cases both albumen and renal tube casts disappear from the urine in a remarkable way when the pregnancy has terminated. Clinically, the two types are so different that many authorities regard them as absolutely distinct renal affections; and some hold that both these two forms, besides differing from one another, are also entirely different from those renal affections which arise from other causes, and which are usually grouped together under the title acute or subacute Bright's disease. It is very probable that the question of whether these pregnancy kidneys are really forms of Bright's disease or not will remain a matter upon which there will always be differences of opinion. The extent to which opinions differ at present is well exemplified in

Sir T. Clifford Allbutt's *System of Medicine*, where the accounts given in different volumes by such authorities as Dr. G. E. Herman and Dr. W. Howship Dickinson respectively, are remarkably at variance. Speaking of the morbid anatomy and histology of the kidneys in the two types of disease under discussion, Dr. Herman says of the first—namely, that in which oedema of ankles and eyelids in the earlier months is the main symptom—which he calls the “chronic renal disease of pregnancy”:

We know nothing of the morbid anatomy of this chronic disease, for it is not fatal. The morbid changes in the kidney can only be found out by examining the kidneys of a pregnant woman who, having the disease, died from some accidental cause, and I know of no such record. A few necropsies have been published, but the accounts are not harmonious, for the evident reason that the patients who died were suffering from forms of renal disease such as occur independently of pregnancy and not from that which depends upon pregnancy.

This does not seem to be altogether fair, for it is as much as to say: “The chronic renal disease of pregnancy is different from that of chronic tubal nephritis due to other causes; therefore, if at a necropsy made upon a patient dying pregnant, or recently pregnant, lesions resembling chronic tubal nephritis are found, the nephritis is not that which pregnancy causes.” It appears to be an argument in a circle in which the conclusion that is drawn is also one of the premisses of the syllogism.

Dr. Howship Dickinson, on the other hand, writes very differently. He says:

The changes which occur in the kidney as consequences of pregnancy may be briefly indicated. They are the changes of heart disease and something more. To passive congestion is superadded an acute inflammation. In an early stage there is much hyperaemia, with obvious fullness of vessels, general redness, and some increase of size. In a case destined to further trouble, a somewhat peculiar form of diffuse nephritis succeeds; the tubes become loaded with epithellum which early takes on fatty change and imparts a yellowish colour, in streaks or otherwise, to the section. The fatty change is not limited to the epithellum, but may be somewhat general. The tubal change is accompanied or quickly followed by interstitial contractile growth, with consequent compression of the tubes, particularly near the surface, and superficial granulation. The condition is one of general nephritis, upon which granular contraction ensues with inordinate rapidity. So early does the contractile process become superadded to, or intermixed with, that of inflammatory swelling that the more bulky results of renal inflammation are excluded; the large white kidney does not, under these circumstances, present itself. The early access of inflammatory change would seem to imply that other causes are at work beside the mechanical, and that these are analogous to those to which other forms of nephritis have been traced. It has been suggested that the kidneys are irritated by some product of pregnancy, possibly an excrementitious result of fetal nutrition. The conjunction of the two morbid agencies, the mechanical and the vital, may account for the greater activity of the disease as compared with the granular kidney of other origin. The puerperal

kidney has a mixed nature ; it is one of diffuse nephritis, upon which granular contraction is rapidly superimposed.

Referring now to the kidneys found at necropsies in cases of fatal puerperal eclampsia, Dr. Herman says :

Very different conditions of kidney have been found. A comparison of the different accounts that have been published shows that they may be divided into three groups. First, disease of the kidney, such as may occur apart from pregnancy, . . . such as lardaceous disease, hydronephrosis, or dilatation of the ureters and renal pelvis. Secondly, in most cases there are changes in the kidneys which to the naked eye resemble those of acute or chronic tubular nephritis. Thirdly, in some cases the kidneys have shown no sign of disease appreciable by the unaided senses. When these kidneys—either those looking like kidneys with acute and chronic nephritis, or those which look healthy—are examined with the microscope, the changes are not those of inflammation but a degeneration like that which is seen in blood poisoning.

These changes have been variously described by various authors, the following being some of the descriptions. Professor Hamilton says :

Judging from the naked-eye appearances, we expected that parenchymatous inflammation of the tubular epithellum in the cortex, passing into a state of fatty degeneration, would be revealed. The first glance at a section of the organ, however, showed conclusively that this was not the case and that the lesion was not an ordinary parenchymatous inflammation. It consisted of degeneration of the epithelial cells of a certain proportion of the tubules in the circumferential aspect of the cortex. The degeneration appeared to be of a colloid nature. The products of these degenerated cells ran down and blocked up, more or less completely, the other convoluted and straight tubules, so as to render them functionally useless, although their tissues were not diseased.

Dr. Charlewood Turner, in a case of Dr. Herman's own, says that the sections—

Show recent degenerative changes of the cortex, without any older or cirrhotic lesions, changes attributable to some toxic matter in the blood. Granular degeneration and swelling of the epithellum of the convoluted tubes, the nuclei of which are invisible, and swelling of the connective tissue throughout, without infiltration of leucocytes. In the medullary tissue the epithellum of the loops and connecting tubes appears normal. Some of the loops contain casts. There is much vascular congestion in this part. The glomeruli appear normal. There is no exudation in the capsules.

Dr. W. J. Fenton, reporting upon a case, says :

Most tubules show what is apparently a running together of the cells, having no definite structure, and having their nuclei obscured, the whole condition of the epithellum being similar to that often found in acute toxic conditions.

And so on—Dr. Herman's conclusion being that—

From these different observations, made by independent pathologists, having no hypothesis to support, it follows that, although the kidneys often look like inflamed kidneys, yet that the lesion of puerperal eclampsia is not nephritis but an acute degeneration such as is caused by blood poisons.



It would serve no useful purpose to give all the multitudinous literature of the subject here. The above quotations sufficiently show that the greatest authorities are in complete opposition as to the nature of the renal changes in the kidney diseases to which pregnancy gives rise. One says that they are not nephritic at all; another that they are nephritic, and nephritic in remarkable degree. The matter must remain largely one of opinion.

The crux of the whole question is: What is nephritis? and What are its different kinds? and even to these questions no absolute answer can be given. The varieties of non-suppurative affections of the kidney included under the heading "Bright's disease" run so much into one another, and so much confusion has arisen from attempts to keep up a distinction between tubal and interstitial nephritis, that it is not to be wondered at that that which some authorities would term a nephritis is refused that title by others.

Dealing with the question from another point of view, it will probably be granted that the kidney lesions which occur during and immediately after scarlet fever are those of nephritis. Whether or not the fibrotic changes which may occur in kidneys which have been inflamed during scarlet fever are also inflammatory is doubtful. It is probably incorrect to speak of chronic nephritis in many instances, for that which is usually referred to as such is the fibrosis which results from former acute or subacute inflammation, the inflammation itself having ceased long since. A similar misapplication is frequent in regard to valvular heart disease: valves which are crippled as the result of former endocarditis are often spoken of as being the site of chronic endocarditis, when what is really meant is fibrosis from former endocarditis, all actual inflammation being now past. Scarlet fever may cause nephritis which, instead of either resolving completely or leading comparatively soon to a fatal result, may leave behind it a fibrosis. It is not this lesion which is at present under discussion, but the acute or subacute lesions which are on all hands allowed the title scarlatinal nephritis.

The kidney which may be found *post mortem* in such cases is very variable in its naked-eye appearances. Sometimes it is a large red, blood-dripping organ, without much blurring of the structural outlines; sometimes it is a large pale kidney, with lack of clear definition between cortex and medulla; more often it is a combination of these two types—a large organ variously mottled with pallid and with crimson streaks and blotches, the general effect being in the direction of redness in some, in the direction of pallor in others, whilst sometimes there is about an equal proportion of redness and of pallor in the mottling. Granted time between the onset of the inflammation and the time of the patient's death, a variable degree of contraction of the kidney will have resulted, with unevenness of the surface owing to irregularity in the distribution of the fibrosis, the colour varying here



again between pallor on the one hand and redness on the other as much as it does in the large kidneys of the earlier stages of the disease.

The microscopical changes are equally variable. Confining attention mainly to the acuter stages, the most striking feature is the obstruction and distension of the tubes, which are stuffed with epithelium, granular débris of cells, and often blood and fibrin, to the more or less obliteration of their channels. Sometimes the fibrin is so abundant as to occupy most of the tubes to the exclusion of their epithelial lining. Often the epithelium of whole groups of tubules seems to have undergone a sort of coagulation necrosis, the line of demarcation between each cell and its neighbour being no longer visible, and the nuclei no longer taking the ordinary stains. In the more protracted cases the periglomerular and intertubular connective tissue shares in the inflammatory process, displaying hypernucleation and proliferation of the connective tissue cells. The degree to which small round-celled infiltration occurs is extremely variable. Sometimes it is almost entirely absent, sometimes it is very obvious, particularly around the glomeruli and in the cortex. The patient may not die until, although there is still actual inflammation present in some places, in others there has been time for fibrosis to have occurred. In short, both the macroscopic and the microscopic appearances of kidneys that are the seat of scarlatinal nephritis are extremely variable, though it can scarcely be said that the different appearances constitute intrinsically different kinds in the inflammation. If any broad rule can be laid down it would be that the sooner after the onset the patient dies the more will the appearances be those of a coagulation necrosis of the epithelium; the longer the patient lives, supposing always that the renal mischief does not entirely resolve, the more will be the connective tissue change, first that of hypernucleation, and finally that of fibrosis.

If the description that has been given of the acute and subacute changes in the non suppurative renal diseases of pregnancy be now recalled, it will be found that these are extremely similar to those that occur in connexion with scarlet fever. If the scarlatinal changes are to be termed nephritis then those associated with pregnancy are surely nephritis too. There have been in Guy's Hospital of recent years 4 fatal cases of the oedema type and 15 fatal cases of the eclamptic type of renal trouble in pregnancy out of a total of 71 cases of the former and 51 cases of the latter. There is little need to recount the changes that were found at the necropsies, because there is little to add to the descriptions already given above. If the kidneys themselves or microscopical sections of them had been mixed up amongst a large number of different scarlatinal nephritis kidneys and their sections, it would have been next to impossible to have gone through them and sorted the pregnancy kidneys from the scarlatinal. Large red, large mottled, large pale, contracting red, contracting mottled, and contracting pale kidneys were all re-

presented, with a predominance of the large mottled and large pale kidneys in the eclampsia cases and of the contracting kidneys in the oedema cases. There were great variations in the microscopical appearances in different cases also. Sometimes cloudy swelling or coagulation necrosis of the epithelial cells in the cortex was the main thing; sometimes even in the eclampsia cases there was hypernucleation of the connective tissue as well. In the oedema cases there was a variable degree of fibrosis, mature and immature, which occasionally reached an extreme degree even in kidneys that were not very obviously contracted. It would seem that every kind of change which may be found in scarlatinal nephritis may also be found in these kidney affections of pregnancy. I therefore range myself with those who regard these kidney changes in pregnancy as essentially similar in kind to those which may occur in scarlet fever, and I believe that there is no intrinsic difference, but only one of degree and acuteness, between the renal changes in eclampsia cases and those in cases where renal oedema is a prominent symptom less late in the pregnancy.

#### *The Cause of Pregnancy Nephritis.*

It is not possible to say precisely what is the cause of the nephritis in pregnancy. It is generally believed to be a toxin—that is to say, a poison of unknown nature—elaborated during pregnancy. To term the changes in these pregnancy kidneys “toxic” does not imply that they are intrinsically different from those of scarlatinal nephritis, where the precise cause, being equally unknown, is termed toxic too. There are doubtless many different substances which can cause similar inflammatory lesions in the kidneys. Pneumococci have been recovered from these organs in cases of acute non-suppurative nephritis associated with lobar pneumonia. Streptococci have been recovered in a similar way from some scarlatinal nephritic kidneys. Cantharides, turpentine, and oxalic acid can cause very similar renal changes. It is more than likely that in certain cases pregnancy gives rise to a poison of some kind which in turn is the cause of the nephritis.

Nothing is really known as to why in some cases eclampsia should be the prominent feature, whilst in others oedema is marked and eclampsia absent, and whilst in yet others both occur. The parallel with scarlet fever nephritis still holds good in this respect, however. There are cases of scarlatinal nephritis in which oedema is entirely absent, and uraemic symptoms are the first to attract attention, whilst there are other cases in which oedema is a marked feature without uraemia. There is an admirable paper upon the subject by Dr. F. M. Turner.<sup>1</sup>

Notwithstanding all the work that has been done upon uraemia its pathology is still unknown. Of late years attention has been directed less exclusively to the kidneys in the study of the subject, and there is some evidence to

show that the liver as well as the kidneys may play an important part in the origin of uraemic or eclamptic symptoms. The liver is nearly always abnormal in these cases, the chief changes being cloudy swelling, fatty change, and acute necrosis of the hepatic cells. It would not be surprising if the liver condition had something to do with uraemia, seeing that if jaundice were deducted from the later symptoms of acute yellow atrophy of the liver, the clinical picture of the latter would not be very unlike that of uraemia.

Before leaving the question of whether or not the renal lesion of eclampsia is really similar in kind to the renal lesion of the cases where general oedema is the main symptom, it may be of interest to note that 4 out of the 71 cases who were admitted for the oedema type of nephritis in association with pregnancy had suffered from typical acute eclampsia in a former pregnancy. Eclampsia is not so common that this can be a mere coincidence. If the same patient is liable to acute eclampsia in one pregnancy and then to the oedematous form of nephritis without eclampsia in a later one, it is very suggestive of there being a relationship in kind between these two clinical forms of renal disease. If these were cases in which the oedema type of nephritis had come first and then eclampsia in a later pregnancy the argument would not be so good, though there are cases of this kind too. The 4 cases referred to had never had symptoms of nephritis apart from pregnancy; their first symptoms of renal trouble were those of puerperal eclampsia towards the end of their first pregnancy. Recovery from this appeared to be complete, and in a subsequent pregnancy there was the nephritic type of oedema associated with albumen and renal tube casts in the urine and without eclampsia. The renal symptoms and urinary abnormalities again resolved after the later child was born.

It would be interesting to trace the after-histories of all the cases of eclampsia that have recovered for the time being and note what happened later. The writer has tried to do this with hospital patients, but the number of cases lost sight of is so great that the statistics obtained so far are too small to be of value. This would be a subject very suitable for a collective inquiry. The cases that have been traced show that puerperal eclampsia has recurred in some without necessarily proving fatal; that in others, as has been mentioned, renal oedema without eclampsia has taken its place in a subsequent pregnancy; whilst others, again, having recovered from eclampsia, have borne subsequent children without either oedema, albuminuria, or eclampsia. It is not improbable that the same would be true of scarlatinal nephritis if scarlet fever could recur in the same patient as often as pregnancy can.

Returning now to a consideration of all the cases together, they are found to bear out entirely what has been noted by others in regard to: the relatively better prognosis in the oedema type of pregnancy nephritis as



compared with the eclamptic; the high proportion of primiparae amongst the eclampsia cases and the preponderance of multiparae amongst those who develop the oedema type of nephritis; the relatively high percentage of cases in which albuminuric reinitis occurs; the relatively greater severity of the symptoms when the uterus contains twins; and the liability for the children to be born prematurely or dead, or for them to die soon after birth.

*The Immediate Maternal Mortality.*—Out of 71 patients with renal oedema and no eclampsia 4 died whilst in hospital, an immediate maternal mortality of 5 per cent., whereas out of 51 cases of puerperal eclampsia 15 died—an immediate maternal mortality of 29 per cent. This is a relatively small mortality as compared with that of acute uraemia not associated with pregnancy.

*The Number of Previous Pregnancies.*—Of the puerperal eclampsia cases 76 per cent. of the patients were primiparae; of the remainder most had had only one previous child, but in 2 cases there had been ten and twelve previous pregnancies respectively. Of the cases with renal oedema and no eclampsia, on the other hand, only 36 per cent. were primiparae, 64 per cent. having borne a former child or children, whilst a considerable number of the multiparae had had from four to twelve pregnancies without evidence of nephritis before. Leaving the eclampsia cases aside, as being of less interest to physicians, it is found on analysing the 71 cases in which there was renal oedema without eclampsia that 70 per cent. had never had symptoms of renal disease until the time when they developed during the pregnancy; that 10 per cent. had passed through a former pregnancy without symptoms of nephritis, but subsequently developed them when not pregnant, and suffered from an increase in the symptoms during a later pregnancy; that 7 per cent. had had acute nephritis before they were married and suffered from recrudescence of that trouble during pregnancy; that 6 per cent. had had eclampsia with a former pregnancy and now had symptoms of ordinary nephritis during pregnancy; that 6 per cent. had had symptoms of nephritis during a former pregnancy, recovering between whiles, but exhibiting the nephritic symptoms again when subsequently pregnant (in one of these cases nephritis with oedema, but without eclampsia, had recurred with each of four successive pregnancies); and that 1 per cent. had had no symptoms of nephritis during pregnancy and had had no eclampsia, but developed the symptoms of acute nephritis, with general oedema, during the puerperium.

As regards the month of pregnancy at which the renal trouble became manifest, that of eclampsia was, as all observers agree, in the latest months or immediately following labour; whereas in the cases where renal oedema was the main symptom the onset was at any time between the second and the eighth month, the trouble manifesting itself about the fifth or sixth month in the majority of cases. In this connexion it might



be asked : If a pregnant woman develops evident oedema of renal type, with albumen and tube casts in the urine, during the eighth month of pregnancy, what is the likelihood that she will also have eclampsia ? It would require a larger number of cases than the above for any absolute answer to be given to this question. It is fairly clear that if nephritis with oedema develops in the early or middle months of pregnancy it is quite exceptional for eclampsia to occur when the pregnancy is more advanced. It is also quite clear that the majority of cases of eclampsia have little or no oedema. Thus in 49 per cent. of the eclampsia cases there was no oedema at all ; in 35 per cent. there was definite, though slight, oedema of the face and ankles ; but in 8 cases, or 16 per cent., the general oedema was extensive, though it only developed in the later months.

Amongst the renal cases in which no eclampsia occurred there were nine in whom generalized oedema developed for the first time during the eighth month or later. There were thus 17 cases in whom extensive renal oedema first appeared in the eighth month, 8 of them subsequently developing eclampsia and 9 of them not doing so. It seems, therefore, that a broad answer to the question propounded above is, that when renal oedema first develops as late as the eighth month of pregnancy, the chances as to whether the patient will suffer from eclampsia or not are about equal.

#### *Albuminuric Retinitis.*

It is generally allowed that albuminuric retinitis in these pregnancy kidney cases is more common than it is in other forms of nephritis. The above cases conform with the general conclusions arrived at by others. Unfortunately, there was not an ophthalmoscopic record kept in every instance. Of the 71 cases without eclampsia 13 had albuminuric retinitis, two dying ; 10 had no albuminuric retinitis, none dying ; and in 48 cases the condition of the eyes is not noted. Even if it be assumed that there was no albuminuric retinitis in all of these, which is improbable, the incidence of the retinal changes is nearly 20 per cent. ; whereas in 312 consecutive cases of chronic nephritis not associated with pregnancy the incidence of the retinitis was 11 per cent.—14 per cent. in those diagnosed as chronic tubal and 9 per cent. in those thought to be chronic interstitial nephritis.

It is generally acknowledged that albuminuric retinitis is less likely to occur in acute Bright's disease than it is in chronic ; nevertheless, it was well marked in 3 of the eclampsia cases, 2 of them dying. It was absent in 9, of whom none died ; and there is no mention of the retinae in the remainder.

Amaurosis was present in several cases in which the optic discs and retinae were normal.

It has been said that pregnancy cases with albuminuric retinitis have a less unfavourable prognosis than have others with a similar lesion. This is perhaps true to the

extent that in a few instances the retinal mischief has been known to disappear again after the pregnancy is over. In at least one of the above cases in which albuminuric retinitis was well marked during pregnancy the albuminuria, the oedema, and the retinitis disappeared entirely after the child was born. Nevertheless, the presence of the retinal changes is a sign of extreme gravity even in the pregnancy cases, the immediate mortality amongst the 16 cases who had it being 25 per cent.—15 per cent. in the non-eclamptic cases and 66 per cent. in those who had eclampsia.

### *The Effect of Twins.*

The deleterious effect of twin pregnancy upon the kidneys is more marked in the eclampsia cases than it is in those with general oedema without eclampsia. Amongst the 71 cases of the latter there was not one of twin pregnancy, whereas amongst 51 of the former there were twins in 4; that is to say, in 8 per cent. The normal proportion of twin to single pregnancies is as 1 to 80, so that the incidence of twin pregnancies in eclampsia cases is more than six times greater than the average. This is precisely what has also been quoted by Schauta,<sup>2</sup> Hofmeier,<sup>3</sup> Löhlein,<sup>4</sup> Schreiber,<sup>5</sup> and others, whose conjoint statistics show that in between 7 and 8 per cent. of eclampsia cases twins are present. This remarkable fact strongly supports the view that the nephritis is due to a toxin elaborated by the placenta or by the fetus, for, as Dr. Herman and others point out, the mere bulk of the uterus will not account for it. "Nothing like eclampsia is ever met with in cases of abdominal tumours—ovarian cysts, uterine fibroids, and so forth—which sometimes get much larger than any pregnant uterus. The frequency of eclampsia with twin pregnancy arises from the presence of two children in the womb and not from mechanical distension of the abdomen."

### *The Effects of the Nephritis upon the Child.*

Whether it is that the influence of the nephritis upon the fetus is bad or that the poor condition of the fetus is in some way the cause of the nephritis is a moot point. The fact, however, that some of the children are born healthy and live to grow up notwithstanding the renal trouble in the mother would seem to indicate that in the other cases the fetus suffers because the mother has nephritis rather than vice versa. All statistics show a high mortality amongst the children and those under discussion form no exception. Leaving the eclampsia cases out of account, the other type of patients show that in 18 per cent. of the cases the child was born too premature to live; in 23 per cent. the child was born near to, or at, term, but dead; whilst in the remaining 59 per cent. the child was born alive, but in a number of instances with too little vitality to continue to live long.

### *Treatment.*

It is not the province of these lectures to enter upon treatment at any length, so that but a few words will be said about it. Clearly the treatment of an eclamptic case lies mainly with the obstetrician. That of the nephritis of the earlier months of pregnancy, however, calls for immediate obstetric measures in but a few cases. Rest in bed, with medicinal, dietetic, and other measures precisely similar to those employed in other cases of acute or subacute nephritis, ameliorates the renal symptoms in many of the cases. The oedema and the albuminuria may thereby almost disappear before the end of pregnancy is reached. The average patient of this kind does better when treated upon the same lines as a non-pregnant case than if obstetric measures for the termination of the pregnancy are recommended and adopted. If, however, the renal mischief increases instead of diminishing, as is sometimes the case, notwithstanding all medicinal treatment—particularly when the latter has not been adopted and insisted upon at the very beginning of the trouble—the case will probably require the assistance of an obstetrician before term, although the relief to the nephritis after an artificial termination of the pregnancy is not as a rule so rapid as it is after natural delivery.

### PREGNANCY IN PATIENTS WHO HAVE ONLY ONE KIDNEY.

Seeing that so much stress has been laid upon the renal affections that pregnancy itself may cause it might well be asked whether a patient who for one reason or another has had one of her kidneys removed ought to be advised not to marry. It must be remembered that although pregnancy sometimes gives rise to nephritis or to pyelo-nephritis the total proportion of all cases in which it does so is exceedingly small. Moreover, it is well known that after excision of one kidney the other, if healthy, has a very remarkable power of hypertrophying by way of compensation. Such a single kidney is seen in the *post mortem* room now and then, and it may weigh nearly as much as two ordinary kidneys. It would be expected, therefore, that if there was no evidence of disease in the remaining kidney, and if the patient was otherwise in good health, pregnancy might be incurred without any untoward symptoms whatever. This is, in fact, what Mr. G. E. Twynam<sup>6</sup> has found to be the case. It may be added that since the greater strain is put upon the right kidney during pregnancy the case is more likely to do well if it is the left kidney that remains; and, further, that since compensatory hypertrophy of the kidney must take some time to become complete, a year or more should elapse between the nephrectomy and the occurrence of pregnancy in any given case.<sup>7</sup>

### TETANY AND PREGNANCY.

Another condition of which pregnancy seems to be one of the causes is tetany. One of the most interesting



points in regard to the association of pregnancy with tetany is perhaps its apparent rarity in Loudon. There does not seem to have been a single case of the kind in Guy's Hospital during the last thirty years. The writer has not seen a case of the association, though he has seen several instances of tetany in adults, chiefly in conjunction with gastric lesions. Incidentally, as a point which possibly supports the toxic theory of the disease, it may be mentioned that more than one case excreted quantities of diacetic acid and acetone in the urine. It is well known that both these substances appear in the urines of many cases of gastric disorder quite apart from tetany, and that they also appear in conditions of starvation, so that possibly the gastric disorders lead to acetonuria, partly or wholly as the result of semi starvation. Nevertheless, in an instance recorded by Dr. David Foreyth,<sup>8</sup> the paroxysms of tetany in a patient who also had evidence of gastric ulceration were always associated with an increased degree of acetonuria. It would be interesting to know whether diacetic acid and acetone were also present in the urine in cases of tetany associated with pregnancy or in those following operations upon the thyroid gland; and, further, whether large doses of sodium bicarbonate had any beneficial effect upon the symptoms and course of the tetany, as might be the case by analogy with the treatment of acidosis in cases of diabetes mellitus.

That pregnancy and tetany are not all generally related to one another as cause and effect is further shown by the comparatively small amount of literature there is upon the subject. One of the best known monographs about it is that of Frankl-Hochwart. From this and from other papers one learns three particularly interesting points about the disease—namely, first, that in places where it occurs at all it bears a remarkable relationship to the time of year; the great majority of the cases arise in the late winter and early spring. Out of 59 cases collected by Frankl-Hochwart<sup>9</sup> 39 occurred in January, February, March, or April, whilst only 13 occurred exclusively in the remaining eight months of the year. Secondly, that there is a noteworthy tendency for the disease to be almost epidemic. There is a little difficulty in interpreting some of the accounts, for the disease was undoubtedly diagnosed erroneously in years gone by. Epidemic cerebrospinal meningitis was formerly confused with tetany, for example. Hysteria affecting many individuals of a township, analogous to that of the dancing Dervishes or to that of the chorea of the ancients, constitutes another difficulty. Even allowing for this, however, the records show clearly that in places where tetany occurs there are some years in which the cases are quite numerous, and then others when the disease almost disappears from the neighbourhood. In Paris, for example, where the tetany of pregnancy used to be quite frequent, it is now said to be a condition of great rarity. Thirdly, in correspondence with the above, it appears to be a disease of extremely

local distribution. Very rare in London, and apparently throughout Great Britain, formerly common in Paris and now rare there, rare throughout America, the two places where it seems to be the reverse of rare are Heidelberg and Vienna. It appears to be endemic in these two cities. It by no means follows, of course, that it is microbial in origin. It is well known that such diseases as cirrhosis of the liver or acute gout, common though they are in some places, are quite rare in others, although there is not yet any proof that either of these is of bacterial origin. There is no reason to suppose that the tetany sometimes associated with pregnancy differs essentially from adult tetany due to other causes. There is no need to discuss its general symptoms here, for they are well known.

### *The Pathology of Tetany.*

The pathology of the condition is obscure, though there is much evidence to show that a toxin, and possibly not always the same toxin, is at work. The morbid lesions that have been described have chiefly been changes in the anterior cornual cells of the spinal cord and the corresponding cells in the medulla oblongata. Such changes would agree with the altered electrical reactions noted in the muscles during life. There is no complete reaction of degeneration, for excitability to the faradic current is retained; but with the galvanic current, instead of the kathodal closure contraction being more easily obtained than the anodal closure contraction, there is an altered polar response which may be summarized by saying that anodal closure contraction and anodal opening contraction are both obtained more readily than kathodal closure contraction. The changes in the spinal cord cells do not seem to be permanent, for the majority of the cases get perfectly well, though there is a tendency for the tetany to recur in several different pregnancies, not necessarily successive, in the same person. The other points that may be of interest are, briefly, the following. The patient usually escapes during the first half of pregnancy, the affection developing in the later months as a rule, though it occasionally shows itself earlier. The spasms are rarely met with during labour—a remarkable point, seeing that they are so readily produced by muscular efforts at other times. They may occur for the first time during lactation, though this seems to be less common than for them to arise during pregnancy, and then continue during lactation. If they occur during lactation it is clearly impossible for the mother to suckle the child, for she is unable to hold it securely. It is necessary to feed the baby artificially, not only for its own sake, but also because it leads to the more rapid subsidence of the tetany in the mother. The treatment of the condition is similar to that of tetany in non-pregnant persons. Finally, the tetany in the mother seems to exert less ill-effect upon the fetus than might be expected.

We may now leave the medical diseases of which pregnancy is itself the exciting cause, and pass on to the discussion of other medical affections which, though not actually caused by the pregnancy, may yet arise or be already present in a pregnant woman. There is hardly a medical disease, from a common cold to a cancer, that may not be thus present, and it is of essential importance to know in what respects, if any, the prognosis and the treatment in the case of a pregnant woman suffering from such intercurrent malady differ from the prognosis and the treatment in other cases. It is manifestly impossible to discuss every such disease in the time at our disposal; many must be left unmentioned.

#### APPENDICITIS IN ASSOCIATION WITH PREGNANCY.

The question of appendicitis is always one of interest. What is the influence of pregnancy upon appendicitis and vice versa? This would be an excellent subject for a collective inquiry. The number of cases of pregnancy in association with appendicitis seen by a single individual is not likely to be great, and the cases that can be collected from the literature are almost necessarily those which are the more severe. The mild cases, which get better without anything very active being done, escape publication, and a collective inquiry which would cover all cases, whether mild or severe, would probably lead to conclusions that could not but be helpful to all.

There is a certain amount of literature upon the subject, some of which has been collected by Mr. George Heaton<sup>10</sup> of Birmingham General Hospital. One of the chief difficulties in connexion with the matter is that of diagnosis. Inflammatory and other lesions of the right Fallopian tube or ovary may simulate appendicitis very closely. The ordinary vomiting of pregnancy may be regarded as the whole trouble when there is really appendicitis, whilst, on the other hand, when a special outlook is being kept for appendicitis, the latter may be diagnosed when none exists. The difficulties that may arise when the lesion is really in the kidney—the pyelonephritis of pregnancy—have already been discussed, and in every case of suspected appendicitis in pregnancy the urine should be carefully examined with the microscope for pus corpuscles. The pains, again, may be referred to the abdomen when the real mischief is in the chest. Indeed, the diagnosis of appendicitis in a pregnant woman is beset with all the difficulties that occur in non-pregnant cases, together with others peculiar to pregnancy. Assuming, however, that the difficulties of diagnosis can be overcome by experience, the questions which arise are—Does pregnancy predispose to appendicitis when there has been no previous attack? Does pregnancy in a patient who has formerly had appendicitis without operation render her particularly liable to another attack during or after the pregnancy? Does the coincidence of pregnancy with appendicitis make the latter more severe than it



is in average cases? Does appendicitis in the mother render the pregnancy more liable to terminate prematurely, and does it militate against the life of the child if the attack occurs when the latter is of viable age? Should the treatment of the appendicitis be precisely similar to that of corresponding attacks in non-pregnant persons, or should the physician's advice be more in the direction of inviting surgical assistance sooner, or more in that of continuing expectant treatment as long as possible in these cases? Should obstetric aid for artificially terminating the pregnancy be sought in any of these cases? These are very vital questions, and yet it is by no means easy to answer them. It may be urged that no definite rules can be laid down and that the action to be taken in each instance that arises must be decided entirely upon the merits of the particular case. This is true to a considerable extent; but when it is borne in mind that very different interpretations are put upon these "merits of the case" by different observers, even in cases of appendicitis in non pregnant persons, it becomes evident that it is still more difficult to decide what is best to be done in cases that are at the same time pregnant.

In answer to the first of the above questions it would seem that pregnancy does not predispose to a primary attack of appendicitis. Amongst all the patients that have been in Gay's Hospital suffering from appendicitis during the last twenty-seven years only one was at the same time pregnant. She was a woman, aged 24 years, who had had no former attack, who had had no previous child, and who was six and a half months pregnant when she was suddenly seized with acute appendicitis of moderate severity. The trouble was localized from the first with the usual fullness in the right iliac fossa. Premature labour came on spontaneously a day or two afterwards, and the appendicular trouble rapidly resolved without operation.

The second question receives the following answer from Mr. Heaton: "If a patient have previously suffered from the complaint and afterwards becomes pregnant, the pregnancy may light up another attack. This it probably does by stretching or breaking down old inflammatory adhesions as the uterus enlarges and rises out of the pelvis. . . . On careful questioning it will often be found that there have been one or several previous attacks, though in some cases they have been of so mild a character as to have been almost disregarded. . . . Some surgeons would in every case remove the appendix in women immediately after an attack of appendicitis, if they be of a child-bearing age." It is manifestly of the greatest importance to have a clear answer to the question and to know whether the above views are correct or not. A young woman might contemplate marriage, and, having had one attack of appendicitis when she was a girl, and having recovered from it without operation and having had no symptoms of it since, she might ask the advice of a physician as to

whether she ought to have her vermiform appendix removed before her marriage or not. She might be loth to undergo the operation and yet willing to follow the advice that might be given. Ought the operation to be advised in such a case or not? The answer can only be given when the results in a large number of such cases in whom no operation has been done have been collected and analysed. I have attempted to follow a number of hospital cases in this way, but to be of value the statistics obtained in a similar way by many different individuals should be put side by side and compared; the results found so far seem to indicate that there is no particular liability for pregnancy to light up fresh appendicular trouble in cases where the former attack occurred years before and appeared to resolve completely. The fact that a girl with ordinary appendicitis may someday become pregnant and might then have a recurrence of the trouble, may doubtless be an additional argument in favour of appendicectomy during convalescence from the attack, but if a patient has not had that operation at the time and has had no return of the symptoms since, the chances of her developing fresh appendicitis later when she becomes pregnant seem to be sufficiently small to warrant the advice that she needs no operation previously to marriage. If, on the other hand, a woman has her first attack of ordinary appendicitis after marriage, at a time when she is not pregnant, and the question arises as to whether she should have her vermiform appendix removed when the acute phase of the attack has passed, the fact that she might become pregnant very soon would seem to be a very real ground for advising that the operation should be done. Although there seem to be practically no statistics upon the subject, pregnancy arising within a few months of an attack of appendicitis would be very liable, one would think, to stretch and break down the immature adhesions in the way that Mr. Heaton describes and lead to a recurrence of the trouble at a time when it would be particularly unfortunate. For the same reason it would be unwise for a young woman who had had appendicitis, not years ago but within the last few months, to get married; and such a patient would probably be advised to have appendicectomy performed, even though for a similar state of affairs in a man the operation might not be essential.

The answer to the third question—namely, whether or not the co-existence of pregnancy makes an attack of appendicitis more severe than the average—cannot be given until, by some process of collective inquiry, all the milder as well as the more severe cases can be collected. This is not at present possible, for the more striking cases become published, the simpler remaining in the background. The proportion of mild to severe cases is thus lost sight of; consequently the severity of appendicitis during pregnancy is very apt to become exaggerated. Nevertheless, those who have seen cases give it as their personal

opinion that pregnancy is a complication which greatly increases the risks and dangers of the disease. The attack may occur at any stage of the pregnancy, as early as the sixth week and as late as the eighth month. The illness may be of all degrees of severity, from transient appendicular colic to the acute fulminating appendicitis which proves fatal in a few hours. In mild attacks, during the early months of pregnancy, the inflammation may completely subside and pregnancy go on uninterruptedly to term. "Owing, however, to the increased blood supply and to the congestion of the parts due to pressure of the enlarging uterus," cases of appendicitis in pregnancy seem to run an unusually rapid course. Though some subside, the majority, if left, seem to go on to suppuration, and the further advanced the pregnancy the more likely this seems to be.

The danger to the mother's life does not cease with the opening of the abscess, for even after drainage of the cavity in the later stages of pregnancy, or in cases where miscarriage has taken place already, a septic salpingitis or endometritis may be set up with a further liability of extension to the peritoneal cavity. As regards the effects upon the fetus, the latter was born dead in 90 per cent. of the cases collected by Abrahams.<sup>11</sup> When pus forms in the later months of pregnancy miscarriage almost invariably takes place whether operation be performed or not. Even in cases where no pus is proved to have been present miscarriage or premature labour is more common than is the rule in healthy cases. It is not surprising that an untoward ending of the pregnancy is so frequent when one considers that the enlarged uterus is almost certain to be in contact with the inflamed tissues and to form one wall of the abscess cavity when pus is present.

The answer to the question of whether or not the treatment should be different to that of appendicitis in non-pregnant cases seems to be this: That, upon the whole, operative measures should be accelerated rather than postponed in these pregnancy cases. There are, of course, quite mild cases in which it is better to do nothing active; but in cases of the next degree of severity, where if the patient were not pregnant it might be thought best to wait, the opinion seems to be that operation should be advised on the very ground that the patient is pregnant, particularly in the later months of pregnancy. Doubtless this will not be the opinion of all,<sup>12</sup> but the reasons given for it seem sound; in the first place, owing to the vascularity of the parts, pus is even more likely to occur in these cases than it is in others; in the second place, the prospect as regards the child is so poor in any case that the course followed should be almost exclusively that which is in the greatest interests of the mother; and, in the third place, the emptying of the uterus by spontaneous miscarriage or premature labour is so likely to occur and with it a rending open of a previously localized inflammation, with



consequent spread to the general peritoneal cavity, that it is very dangerous to wait.

The foregoing argument gives the answer to the last of the questions that were put above. It is in the last degree undesirable that obstetric measures for terminating the pregnancy artificially should be resorted to for fear of breaking down adhesions that are helping to localize the inflammation.

Pinard<sup>13</sup> has collected 45 cases of appendicitis complicating pregnancy, the diagnosis being confirmed in 30 by operation or *post-mortem* examination. He concludes that appendicitis may attack a pregnant woman at the beginning or at any time during pregnancy; that in the majority of cases it causes abortion, the reason for which is that the fetus becomes infected with the *Bacillus coli communis*, this organism being recoverable from its blood; that every type of appendicitis may occur, the severer cases predominating; and that operation should be advised as early as possible, both for the mother's sake and with a view to diminishing the chances of fatal infection of the child by the *Bacillus coli communis*.

If a pregnant woman develops an attack of appendicitis that is in any degree severe, the statistics that are available all indicate that the best chance of saving both the mother and the child is by early operation.

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- <sup>3</sup>Zeit. für Geburt. und Gynäk., vol. vi. <sup>4</sup>Ibid., vol. vi. <sup>5</sup>Arch. für Gynäk., vol. li.
- <sup>6</sup>BRITISH MEDICAL JOURNAL, February 12th, 1898, pp. 423-425; and West London Medical Journal, 1898.
- <sup>7</sup>See also Schramm: Berl. klin. Woch., No. 6, 1899. Fritsch: Die Krankheiten der Frauen, Berlin, 1894, p. 98. Israel: Arch. für klin. Chir., v. Langenbeck, vol. xlvii, 1894. Tridondau: Annali di Ostetrica e Ginecologia, July, 1896. C. E. Purslow: BRITISH MEDICAL JOURNAL, 1898, Part I, p. 817. H. E. Maberly: BRITISH MEDICAL JOURNAL, 1898, Part I, p. 604. A. Pauz: Königlichen Ungarischen Aerztevereins zu Budapest February 7th, 1906, p. 11. <sup>8</sup>Guy's Hospital Gazette, 1902. <sup>9</sup>Die Tetanie, Berlin, 1891. See also Dakin: "Tetany in Pregnancy," The Lancet, May 16th, 1891, p. 1103, where all cases recorded up to that date are collected, with references.
- <sup>10</sup>BRITISH MEDICAL JOURNAL, March 4th, 1905, pp. 463-465. <sup>11</sup>American Journal of Obstetrics, February, 1897.
- <sup>12</sup>See also Vinay: Lyon Médical, January 2nd, 1898. Bouillier: Thèse de Lyon, 1897, and EPITOME, BRITISH MEDICAL JOURNAL, No. 442, 1898. Toupet and le Filliatre: Bulletin de la Société Anatomique de Paris, December, 1898. The Lancet, October 11th, 1902, p. 1004. Donoghue: Boston Med. and Surg. Journ., September 4th, 1902. Mixter: Ibid., December, 1891. Mundé: Med. Rec., 1894. New York Med. Rec., 1907, vol. i, p. 880. <sup>13</sup>Semaine Médicale, March 23rd, 1898.

## LECTURE III.

## PREGNANCY IN RELATION TO CERTAIN FEVERS.

MR. PRESIDENT AND GENTLEMEN,—The next variety of cases that deserves consideration is that in which the mother, being at the time pregnant, develops one of the commoner fevers. Generally speaking, the pregnant state seems to confer some degree of immunity, the reverse being true of the puerperium. Scarlet fever, for example, shows less tendency to attack a pregnant woman than other persons equally exposed to the infection; whereas a woman who has been recently delivered of a child is particularly prone to take the disease if it is in the vicinity. Nevertheless, pregnancy confers no absolute immunity to the specific fevers, and should the patient contract one the question will arise as to what is likely to be the result both as regards the mother and as regards the child.

## TYPHOID FEVER AND PREGNANCY.

Typhoid fever, for instance, may develop during pregnancy. There are a fair number of papers upon the subject, references to several of which have been given by Mr. H. T. Hicks and myself in the *Lancet*.<sup>1</sup> The illness may begin at any period of the pregnancy, and, like typhoid fever in England generally, it is less liable to develop in the summer months than it is in the autumn and winter.

The course of the disease is precisely similar to its course in other persons. Pregnancy does not seem to have any particular influence on the severity of the illness nor upon the prognosis as regards the mother. The death-rate will doubtless vary in different years; in our own cases it was 14 per cent., in Vinay's 17 per cent., and in Duynot's 16 per cent., figures which do not differ widely from those given by the Metropolitan Asylums Board for all cases. The effect of enteric fever upon the pregnancy is, on the contrary, bad. In the majority of the cases abortion or premature labour takes place. This was the result in 85 per cent. of our cases, in 66 per cent. of Vinay's, in 63 per cent. of Martinet's, and in 65 per cent. of Penot's. The reasons for this high mortality amongst the children will be discussed below. Meanwhile it is right to mention, however, that it is quite possible in a minority of cases for the mother to pass through a typical and fairly severe attack of typhoid fever and yet for the pregnancy to continue to term and for the child to be born living and well. This was the case in one

of our patients who developed typhoid fever in the fifth month of her pregnancy, recovered in due course, and was delivered at term of a healthy child who lived to grow up. There is no period of the fever at which a premature ending of the pregnancy seems more likely to occur than at another. The time at which it takes place depends rather upon the month of the pregnancy than upon the day of the fever. If the patient is already eight months pregnant, for example, delivery may occur during the first week or ten days after the onset of the fever; but if the pregnancy has not passed the fifth or sixth month it may continue into the third or fourth week of the fever and yet end prematurely. The mother seems to suffer remarkably little from the labour. Of course, she may already be in an extremely bad way from her typhoid fever, just as any other person might be, and then the prognosis is grave. It might have been expected that even if she had not hitherto been more than ordinarily ill from her enterica, the additional strain of labour must necessarily have made her considerably worse; this, however, is not the case as a rule. The delivery is most often easy and the patient experiences considerable relief. The uterus involutes just as if there were no maternal illness, and the fever usually runs just the same course as if the incident had not occurred.

*Transplacental Transmission of Toxins, Agglutinins, and Bacteria.*

Several points of considerable scientific, if not clinical, interest arise in connexion with the child. The following questions might be asked:—If the child were born dead during the course of typhoid fever in the mother, would it be likely that typhoid bacilli might be found in the fetal tissues; in other words, can typhoid bacilli be transmitted directly from the mother to the fetus? If the child's blood serum were tested by Widal's test, would it be likely to give a positive reaction? If so, does the fetus produce its own agglutinins, or does it receive them ready formed from the mother? If the fetus can and does become infected with typhoid bacilli, does it develop ulceration in the Peyer's patches of its intestine; in other words, can the macroscopic condition of the fetal bowel be relied upon as a certain indication as to whether the fetus is infected with typhoid organisms or not? If the fetus becomes infected with typhoid bacilli, does this happen soon after the mother falls ill? and, if not, how long after the mother's infection is that of the fetus likely to occur? Would the child, if it lived, have a natural immunity to typhoid fever, supposing it had remained *in utero* until after the mother had recovered from her fever? If the fetus is not affected in any of the above ways, or even if it is, are there any other lesions that it is likely to have suffered as the result of the mother's illness—lesions which may show their effects if the child lives and grows up?



It is only possible to give limited answers to some of these questions, and no answer at all to others; but it should some day be possible to give full answers in every case as it came under observation were fully investigated. The difficulty is that one does not always realize at the time the precise points to which attention should be particularly directed, and the cases are sufficiently few and far between to make it difficult for a single individual to investigate any large number of them. Here, therefore, is another subject upon which a carefully directed collective inquiry would be good. The great point about typhoid fever in this respect is that it affords a natural experiment in human beings upon the placental transmission both of chemical substances—the agglutinins—and of bacteria—the typhoid bacilli—simultaneously.

Before entering upon the facts known in regard to the placental transmission of agglutinins and bacteria in typhoid fever itself it will be well to summarize shortly what is known about placental transmission generally. It seems clear, in the first place, that transmission might conceivably take place from mother to fetus in one other way than through the placenta; it might occur via the liquor amnii. Ferrari<sup>2</sup> has shown this to be possible, materials being able to pass from the maternal lymphatics into the amniotic fluid, and thence, by being swallowed, into the alimentary canal of the child. It is generally held, however, that the only path of fetal infection that is at all common is that across the placenta. Dr. J. W. Ballantyne<sup>3</sup> points out how important this fact is in connexion with the site of the subsequent lesions, for the substances so transmitted reach the child by the blood stream, and therefore if bacteria are conveyed to the unborn child they pass first the placenta, then the umbilical vein, then either the liver or the ductus venosus, then the heart, and so are distributed all over its body. The condition is thus one of general blood infection from the onset. The lesions may consequently be different in the child from what they are in the mother. As an illustration of this, Bidone<sup>4</sup> records a case in which erysipelas in the mother gave rise to fungating endocarditis in the child.

In the second place, it is clear that the placenta allows chemical substances to pass across it from the maternal to the fetal circulation; the nourishment of the child is thus conveyed.

In the third place, it is evident that a converse transmission of chemical substances takes place across the placenta from fetus to mother; the child gets rid of the effete products of its metabolism in this way. It has been shown that quite abnormal substances may pass from fetus to mother in a similar manner. Charrin<sup>5</sup> injected diphtheria toxin into animal fetuses *in utero*, the mother dying from the toxæmia. It has been suggested that toxins elaborated by the fetus and absorbed by the mother may be at the root of the herpes gestationis, the nephritis, and the tetany of pregnancy.

In the fourth place, even as regards chemical sub-

stances, the placenta can apparently exert some power of selection; that is to say, whereas some elements and compounds pass from the mother to the fetus with comparative ease, others do so with much less readiness. Porak<sup>6</sup> performed a considerable number of experiments upon guinea-pigs in this connexion; and he found, for example, that whereas copper and lead were easily transmitted to the fetal tissues, arsenic passed across with greater difficulty, whilst mercury, though it reached the placenta and accumulated there, apparently passed no farther. This feature of the placental functions has been termed its "barrier action."

Fifthly, this "barrier action" of the placenta, decidedly limited even in health, becomes still less marked when the mother is ill. Charrin and Duclert<sup>7</sup> showed that the presence in the maternal circulation of certain chemical substances or of various microbial toxins renders the placenta permeable to things which otherwise pass across it with difficulty; in other words, the placental barrier often breaks down when the mother is unwell, and things which would not be allowed to pass across to the fetus if the mother were healthy are then able to do so.

Sixthly, it has been fully established that bacteria can pass from the mother to the fetus via the placenta. There is a good deal of evidence to show that the placenta itself acts to some extent like a filter, and that it may contain an abundance of bacteria before any have escaped past it to reach the fetus. Consequently the fetus seldom contains bacteria in anything like the numerical proportion that the mother's tissues do. Nevertheless, Küss<sup>8</sup> has shown in animals that tubercle bacilli may actually reach the fetus from the mother via the placenta; and other observers<sup>9</sup> have demonstrated the same fact in regard to the bacilli of anthrax and of fowl cholera, the pneumococcus, the streptococcus, the meningococcus, the *Spirillum obermeieri*, and the bacillus of glanders.

It must be remembered, of course, that the experiments that have been made upon the subject have been upon animals; that the placentae of different animals, varying as they do in size and thickness, vary also in the extent to which each exerts a barrier action against this substance or that; and that, therefore, the facts that have been found to be true of animals are not necessarily true of man. However, although the details may vary it is unlikely that the general principles taught by animal experiments do not apply to man. These principles are: (1) that abnormal chemical substances and toxins are able to pass from mother to child via the placenta; (2) that the placenta when healthy exerts some degree of "barrier action," allowing some things to pass less readily than others; (3) that this "barrier action" is not only imperfect but becomes less effective when the mother is ill; and (4) that not only substances in solution but also actual bacteria, even those of the size of anthrax bacilli, can reach the child from the mother.

To return now to the discussion of typhoid fever and

the way in which the child is affected when the mother has the disease. It has been found repeatedly that the typhoid bacilli can cross the placenta, reach the child, and be recovered from the infant's tissues immediately after birth. There are, it is true, many cases in which the bacilli have been looked for and not found. This was so in the case investigated by Mr. Hicks and myself,<sup>10</sup> but negative evidence in many cases counts for little as compared with positive evidence in even only a few. Typhoid bacilli have been recovered from the tissues of the human fetus by such observers as Fordyce, Freund and Levi, Etienne, Bolton, Eberth, Hildebrandt, Giglio, Durk, and Ernst.<sup>11</sup>

The fetal blood stream has been examined by Widal's test in a few cases, and although it has sometimes given no reaction<sup>12</sup> in cases recorded by Fordyce, Chambrelent, Griffiths, Mosso and Danic, Bolton, and Kirton,<sup>13</sup> it gave a positive Widal's test.

No answer can as yet be given to the question whether the fetus produces its own agglutinins or receives them ready formed from the mother, but it would be a most interesting point to investigate further, especially if it could be shown that the fetus did produce agglutinins for itself. There are at least two ways in which light could be thrown upon the question, neither of them very difficult provided they were kept in mind when an opportunity for using them arose.

First, in every case of maternal typhoid fever the child, if stillborn, should be thoroughly examined by cultural methods for typhoid bacilli, whilst at the same time its serum should be subjected to Widal's test. If several cases occurred in which the latter was positive whilst at the same time no typhoid bacilli could be obtained from any of the fetal organs, it would tend to prove that the child could receive agglutinins ready formed from the mother. Apparently no such case has yet been recorded; in every instance in which the child's blood serum gave a positive Widal's test bacilli were either shown to be present also or else they were not looked for.

Secondly, the precise degree of the Widal's reaction should be determined in all such cases both for the mother's and for the child's serum, with a view to ascertaining whether the child's blood will sometimes give a positive reaction in greater dilution than the mother's does. If, for example, a positive reaction were given by the child's serum diluted 500 times whilst the mother's serum failed to give it when diluted more than 200 times, it would be some evidence in favour of the agglutinins being formed, in part at least, by the child itself. These are points upon which observations are still required, and it is only now and then that an opportunity for making the investigation presents itself.

The next question—namely, whether a child that has become infected by typhoid bacilli *in utero* is likely to exhibit macroscopic evidence of this in the form of ulcerated Peyer's patches similar to those of adults suffering from



typhoid fever—may be answered both yes and no. In a few cases, such as those recorded by Charcellay,<sup>14</sup> definite ulceration of the fetal Peyer's patches has been noted. Such macroscopic lesions, however, are quite the exception, and the great majority of the children whose blood and organs have yielded typhoid bacilli on cultivation, or whose serum has given a positive Widal's test, have shown no such macroscopic lesions in the bowel. The absence of intestinal ulceration, therefore, is no proof that the child has not become infected by typhoid bacilli *in utero*. Consequently, it is essential to cultivate from the fetal organs if it is desired to find out whether the fetus has become infected from the mother or not.

The fourth question, as to whether the child, if it lived, would have a natural immunity to typhoid fever, is unanswerable at present. It would be possible to give an answer if a watch were kept upon all children born alive from mothers who had suffered from, and survived, typhoid fever during the pregnancy. If even only one or two such children subsequently developed typhoid fever it would make it probable that none of them had an immunity, acquired either actively or passively *in utero*. It is a point that is not of any great clinical importance, because the number of living persons concerned is very small; but from a scientific point of view it would be of great interest to obtain an answer to the question, seeing that it bears upon the very complex subject of immunity and constitutes a natural experiment in man. It may, perhaps, be mentioned that the presence or absence of a positive Widal's reaction in the fetus is by no means synonymous with the presence or absence of immunity to typhoid fever. The agglutinins upon which the Widal's test depends disappear rapidly from the blood after typhoid fever in the great majority of cases, as Dr. M. G. Loulsson and myself<sup>15</sup> have shown. Acquired immunity to the disease does not disappear in this way. Consequently the fact that Widal's test is negative in a child born of a mother who has had typhoid fever during her pregnancy does not prove that the child is not immune to typhoid fever. The longer before the child's birth the mother recovered from her illness the less likely would the infant's blood be to give a positive reaction, if one may argue by analogy with adults, in whom the rapidity with which Widal's test, having been positive during the fever, becomes negative again a few weeks or months later is often remarkable.

Next comes the question as to whether or not the child, if it survives in spite of the mother having had typhoid fever during the pregnancy, is likely to suffer in other ways as it grows up. There is a considerable amount of evidence to show that this is very likely to be so, though it would be too much to say that it must be so. Professor Osler<sup>16</sup> has recorded a case in which the mother died from typhoid fever and the unborn child was found to have a large recent blood clot in its brain. Had the infant lived, it

must have exhibited the effects of this lesion, which was apparently due to the mother's illness. Dr. Ballantyne<sup>17</sup> quotes numerous observers who have found "important pathological changes in the fetal viscera, more particularly in the liver, thyroid gland, brain, and suprarenal capsules, which have a far reaching effect upon the post natal life of the offspring. . . . They consist in degenerative and sclerotic alterations unaccompanied by the presence of microbes, but productive of a slackening of body metabolism and lowering of body temperature, along with a tendency to develop bronchopneumonia, gastro enteritis, and infantile atrophy. The same results are produced by other infectious maternal conditions also, and they are probably due to the transmission of toxic principles through the placenta. . . . It has been thought that typhoid fever of the mother in pregnancy may be the cause of intellectual peculiarities in her offspring developed many years afterwards."

### *The Question of Advising Artificial Delivery.*

Before leaving this subject there is one matter of great practical importance that arises from the question of fetal infection, and that is, At what period of the maternal typhoid fever does the fetus become infected with typhoid bacilli? It is held by some bacteriologists that these bacilli are present in the maternal circulation from an early date in the illness, though it has by no means been established that this is an invariable rule. One would like to know precisely when typhoid bacilli are most numerous in the mother's blood, because that would be the time when the fetus would be exposed to the greatest chance of bacterial infection. In our own case<sup>13</sup> the mother died upon the twenty-fourth day and the fetus was not infected. In the cases recorded by others<sup>19</sup> of recent years—that is to say, since the methods of distinguishing the typhoid bacillus from the *Bacillus coli communis* have been rendered more accurate than they formerly were—the examinations were made in five cases when the mother's illness was in its second or third week, and in none of these did the fetal tissues yield typhoid bacilli, whereas in the three cases when the examination was made during the fourth or a later week of the mother's illness the organism was present in the child each time. This number of patients is too small to generalize from, but the results seem to indicate that before the end of the third week of the mother's illness the child is much less likely to have become infected than it is in the fourth or a later week. It seems probable that the prognosis as regards the immediate and subsequent life of the child will be much better if the infant could be born before this bacterial infection occurs. If, therefore, the pregnancy has reached the time when the child is viable, and if for any reason it is much desired that a living child should be born, it would seem that the best advice for the physician to give

would be that of obtaining obstetric assistance for bringing about delivery before the mother's illness had reached the end of the third week. This advice would not be necessary if the mother's interests alone were to be considered, for in her case the prognosis is not materially affected by allowing the pregnancy to take its own course; but if the child's life is a material consideration it would appear to be very risky to allow it to remain *in utero* beyond three weeks from the beginning of the typhoid fever. With each week of the fever the chances that the child will become infected with typhoid bacilli rapidly increase.

#### *Other Specific Fevers in the Unborn Child.*

The discussion upon typhoid fever in conjunction with pregnancy has been somewhat dwelt upon, because, owing to the comparative ease with which both typhoid bacilli and agglutinins can be looked for, the cases afford an admirable field for investigation; they constitute natural experiments in man upon the transplacental transmission of disease upon which there is scope for much more work in future cases. Much might be said about the other specific fevers also, but there is only room for a few words about each here.<sup>20</sup>

Small pox has long been known to be transmissible from the mother to the fetus *in utero*. It by no means follows, of course, that the child has the eruption in every case in which the mother suffers from the disease during her pregnancy. Sometimes the fetus has died before the exanthem could appear upon it. Sometimes the child will be born quite healthy and catch the complaint at birth—a postnatal, and not an antenatal, infection. Sometimes when the mother has had variola early in her pregnancy the latter has continued to term, and the child, though exhibiting no external evidence of having had small-pox, has been noted to possess a natural immunity to the disease in after-life. In quite a number of cases, however, the child has been born with the typical eruption of small-pox upon it. The degree to which the infant is affected is very variable, bearing no direct relationship, apparently, to the severity of the disease in the mother. The stage of the eruption in the child may be almost identical with that in the mother, varying from vesicle to scar according to the length of time the pregnancy has continued after the mother was taken ill. It is noteworthy that the eruption goes through a pustular stage in the unborn child just as it does in an adult; and, as a rule, the size of each lesion is greater than that seen in grown-up people. On the other hand, the duration of the eruption on the skin of the child may apparently be much longer than it is in adults, for in Laurens's case,<sup>21</sup> quoted by Dr. Ballantyne, the mother had small-pox early in her pregnancy, and two and a half months later the premature infant was born still covered with the eruption. Dr. Allan Warner<sup>22</sup> records an interesting case of the same kind.



The mother was taken ill with small-pox upon January 8th when four months pregnant. The eruption appeared upon her on January 11th; by the 23rd the crusts were falling off, and by February 3rd she was quite free from all scabs. Pregnancy continued until the 15th, when miscarriage occurred; twin female children were delivered, both being well covered with a typical small-pox eruption in the pustular stage.

Another very remarkable fact is that the father may have small-pox at the time of conception, the mother may show no sign of the disease, and yet her child may have it *in utero*—a point which seems directly analogous with some cases of congenital syphilis. This opens up a wide field for discussion, but one upon which it is not possible to enter here.

Three further points may be briefly noticed. First, there seems to be no stage of fetal life, from the third month onwards, at which the child may not be born with the eruption upon it. Secondly, even if there is no eruption upon the child's skin it is very possible that, owing to the route of infection being by the blood stream, the lesions might be found upon mucous surfaces, a point which, as Dr. Ballantyne says, deserves full investigation in future cases. Thirdly, it might well be asked, What would be the behaviour of the child in regard to vaccination if the mother had been vaccinated successfully during the pregnancy? It seems clear<sup>23</sup> that two thirds of such children are just like other children and "take" well at the usual time after birth, but that one-third prove insusceptible to vaccination for a short time after birth. The latter cases will, however, "take" six months or so later. It seems, therefore, that there may be a transmission of immune substances from the mother to the child *in utero*, but that even when this passive immunization of the infant by maternal vaccination occurs it is quite transitory. It is therefore no argument against vaccination of the child that the mother has been vaccinated during the pregnancy, though it might be wise to counsel waiting for six months or a little longer before vaccination is performed in order to be more sure of its being successful at the first attempt.

Dr. Cordes has published an interesting case. The mother had small-pox during pregnancy and recovered. The child was born later, and was vaccinated in the usual way, but failed to "take." When it grew up, vaccination was repeated on two further occasions, failing to "take" each time. Soon afterwards the young man went to China, caught small-pox, and died from it. It would seem here as though the mother's small-pox had rendered the child insusceptible to vaccination without at the same time rendering him secure from small-pox itself. Not only was he not secure from the disease, but he took it with fatal severity. The importance of a possibility of this kind is obviously great.

Just as variola may be transmitted from mother to child *in utero*, so may other specific fevers. The total number

of cases in which such a disease as measles coincides with pregnancy is naturally not great, and the number of instances in which the child is born during the stage of the exanthem in the mother is still smaller. The total number of recorded cases of fetal measles is therefore not great, but Dr. Ballantyne<sup>14</sup> describes some and has collected altogether 20. He also records cases of fetal scarlet fever, chicken pox, mumps, pertussis, influenza, rheumatic fever, relapsing fever, yellow fever, cholera, malaria, and even cerebro-spinal fever and anthrax. There is clearly too little time at our disposal to give an account of all of these, but after what has already been said in regard to the transmission of typhoid bacilli from the mother to the fetus it may be of special interest to say a few words about the last two.

A most conclusive case of fetal cerebro-spinal meningitis is recorded by Dr. Ballantyne. The mother died from the disease, the seven months child remaining *in utero*. At the necropsy there was the typical lesion in the maternal meninges, over both the brain and the spinal cord, whilst the meninges of the fetus exhibited precisely similar changes, and the *Diplococcus intracellularis meningitidis* was cultivated separately both from the mother and from the child.

In regard to anthrax, Rostowzew<sup>21</sup> investigated three cases in which the mothers died from the effects of malignant pustule, and he found numbers of the anthrax bacilli in the placental intervillous spaces and in the fetal villi, smaller numbers being also present in the fetal blood and viscera.

There is abundant proof, therefore, that notwithstanding the "barrier action" that the healthy placenta may exert in protection of the child from injurious substances, the barrier may become broken down, or at least passed, as the result of many different diseased states in the mother; and that not only chemical substances in solution but also comparatively large concrete bodies such as bacteria may then gain access to the child. Before leaving this subject a few words may be said as to the effects of some of these fevers upon the mother.

#### THE EFFECTS OF MEASLES UPON THE PREGNANT WOMAN.

Pregnancy does not confer any immunity against the taking of measles. A pregnant woman who has not had the disease should therefore avoid exposure to infection. Should she develop the illness the prognosis as regards herself is good, but there is a considerable danger of abortion or premature delivery during the eruptive stage. It has been suggested<sup>22</sup> that measles affects the mucosa of the uterus as it does that of the nose, pharynx, eyes, stomach, bronchi, bladder, and bowel, causing an inflammatory congestion similar to that which has been observed in some cases of variola, and thereby accelerating miscarriage. If the exanthem stage is past there seems to be little or no danger either to the mother or to the child,

unless the former should develop bronchopneumonia, in which case, owing to the abdominal condition, especially in the later months, the dyspnoea and the repeated attacks of coughing may be a source of greater trouble and anxiety than usual.

#### THE EFFECTS OF PERTUSSIS UPON THE PREGNANT WOMAN.

The latter applies also to whooping-cough during pregnancy. Pertussis in an adult is very apt to be exceedingly distressing in any case, but when it is combined with pregnancy the patient may be in a very pitiable plight. The paroxysms of rapidly repeated cough, each bout sometimes terminating only in the ejection of some of the gastric contents, render the patient abjectly miserable. There is a danger of premature emptying of the uterus in consequence of the extreme and constantly repeated contractions of the diaphragm and abdominal muscles, but otherwise the prognosis is good both as regards the mother and the child.

#### THE EFFECTS OF SCARLET FEVER UPON THE PREGNANT WOMAN.

Scarlet fever arising in a pregnant woman has a relatively much graver prognosis than it has in other cases. The complication is least serious when it occurs early in the pregnancy and when it does not lead to abortion. It is, however, much rarer at this time than it is towards the end of pregnancy—so much so that it has been thought that the pregnant state confers some degree of immunity to it. The converse is true of the puerperium, when the patient is particularly liable to the infection, and whether the scarlet fever begins either immediately before or immediately after labour, not only is the intensity of the disease itself, its rash and its pyrexia, apt to be extreme, but also there is a very great liability to sapraemia, or, still worse, to actual septicaemia from streptococcal invasion. This view is not held by all; indeed, Dr. R. Boxall,<sup>27</sup> in a series of papers before the Obstetrical Society in 1888, contended that scarlet fever begets scarlet fever even in a pregnant woman, and has no relation to puerperal septicaemia. Dr. F. Foord Calger, however, gives it as his opinion, from personal experience, that the conjunction of scarlet fever with present, or recent, pregnancy near to term cannot but be viewed with the gravest anxiety. The maternal mortality varies in different epidemics, but it may be as high as 75 per cent.

#### THE EFFECTS OF CHICKEN-POX AND MUMPS UPON THE PREGNANT WOMAN.

Chicken-pox is often much more severe an illness in adults than it seems to be in children, but there is no evidence to show that its occurrence in conjunction with pregnancy makes it any worse. The prognosis as regards



both the mother and the child is good, though, as has been stated, the child may be born with the eruption upon it if the mother suffers late in the pregnancy.

The same remarks apply to mumps. It is, perhaps, a little surprising that mumps do not act very detrimentally upon the pregnancy, seeing that there is a considerable tendency for the parotitis to be associated with inflammation of the genital organs—ovaritis in woman, orchitis in man. The existence of pregnancy does not seem to render the patient more liable to ovaritis than usual, however, and the pregnancy often continues undisturbed.

#### THE EFFECTS OF DIPHTHERIA UPON THE PREGNANT WOMAN.

The pregnant state confers no immunity to infection by diphtheria, and the disease appears to have a particular virulence in the case of pregnant women. There was a discussion upon the subject in the *Lancet*<sup>28</sup> in 1903, and Dr. Chambrelent and Dr. Michelean<sup>29</sup> have collected together a number of cases in Bordeaux. The statistics available are open to the objection that they are based upon cases taken from the literature, and not upon a consecutive series of unselected cases. Nevertheless, two things seem clear: first, that the diphtheria is particularly prone to attack the larynx in these cases, as in children, rather than the fauces, as in other adults; secondly, that if antitoxin is not employed the mortality is very great. Of Dr. Chambrelent and Dr. Michelean's cases there were 12 who received no antitoxin, and 6 of them died, a mortality of 50 per cent. All their cases in which serum was given recovered. Mr. A. E. Kennedy<sup>30</sup> points out that even the giving of antidiphtheritic serum early will not save every such case; nevertheless, the proportion of recoveries is so much greater when serum is used early than when it is not that it should always be given at the earliest possible moment to a pregnant woman who has diphtheria.

#### THE EFFECTS OF SMALL-POX UPON THE PREGNANT WOMAN.

The effects of small-pox upon pregnancy have been closely observed in an epidemic during which there were opportunities of watching 432 consecutive cases in women under 50, 80 of whom were pregnant.<sup>31</sup> Of the latter, 15 per cent. died, whilst the mortality amongst the non-pregnant women was 11 per cent. The prognosis is, therefore, rather worse when the woman is pregnant, though not so much worse as might have been expected. The statistics are here, but I need not read them. In the 80 pregnant cases confluent small-pox was seen in 4 and haemorrhagic in 6; all 10 died. In the 352 non pregnant cases the confluent form was observed in 3 and the haemorrhagic in 11; 2 of the confluent cases recovered. Two pregnant women died, though their small-pox was of

the mild type. Of the primiparae, 9 per cent. died of the multiparae, 17.25 per cent. The general impression during the epidemic was that there was a tendency for the pregnant women to suffer from a severer type of the disease than the others. The prognosis as regards the child is grave. Of the 80 cases, 23 aborted or had premature delivery; 16 other children were delivered alive in cases where the small-pox was in progress—8 at term and 8 prematurely; only 3 out of the 16 children lived longer than six months. In 2 cases the small-pox eruption was present upon the child at birth.

#### CHOLERA AND PREGNANCY.

Cholera is fortunately of rare occurrence in European countries, but occasionally there are epidemics such as that at Hamburg. Schütz<sup>32</sup> published a complete report of the influence of cholera upon menstruation, pregnancy, labour, and childbed, in the annual report of the Hamburg State Infirmary at that time. He treated 2,500 adult females during the epidemic, and found that cholera shows a marked tendency to affect the uterus. In the cramp stage of the disease uterine bleeding occurs in one-third of the non-pregnant cases. It is not surprising, therefore, that the effects of cholera upon pregnancy are disastrous. One hundred and fifteen of the patients were pregnant at the time they were taken ill with cholera; and Schütz puts this disease upon a level with small-pox in the way it is almost certain to provoke interruption of pregnancy. Kovalsky<sup>33</sup> finds the same to hold good in Russia, where over 80 per cent. of the pregnancies come to an untimely end in cholera patients. The prognosis as regards the mother, bad as it is in many of the cases, is not much worse in pregnant than it is in non-pregnant persons, particularly if the mother is taken ill when the pregnancy is not advanced. There is nothing to be gained by advising steps to be taken to terminate the pregnancy; indeed, convalescence is greatly impeded during the puerperium, and the risk of sepsis is greatly increased, so that the pregnancy should be allowed to continue if it will.

#### PLAGUE AND PREGNANCY.

The above remarks concerning cholera apply with equal force to plague. Pregnant women show no particular immunity to this disease. The prognosis as regards the mothers is no worse than it is in non-pregnant patients, but the disease terminates the pregnancy in the great majority of cases. Dr. B. H. F. Leumann<sup>34</sup> records some instances in which the mothers recovered exceedingly well, but there seem to be fewer statistics in regard to the effects of plague upon pregnant women than there are concerning cholera.

#### MALARIA AND PREGNANCY.

The effects of malaria upon pregnancy are necessarily variable, both on account of the varying severity of the

malarial attacks in different patients and in different climates, and also because the immediate surroundings of the patient are so very diverse in different parts of the tropics. It is not easy, therefore, to summarize them in any but quite a broad way. There are papers by Italian observers<sup>35</sup> upon the subject and a few in English, notably one by Mr. F. H. Edmonds<sup>36</sup> of Demerara. The general conclusions which may be drawn are that malarial cachexia has almost no influence upon pregnancy and its course; that in mild cases of intermittent malaria pregnancy usually continues normally to term notwithstanding the ordinary attacks of fever in the mother; that in cases where the maternal temperature reaches 104° F. during the attacks abortion takes place in a large proportion of cases; whilst in the bilious remittent type of the disease not only is the pregnancy almost certain to terminate prematurely, but also the child, even if it has reached a viable age, is nearly always dead, and the prognosis as regards the mother is distinctly graver than it would be in a non-pregnant person with the same degree of malarial illness. There is a very great tendency for both the fetal movements and the uterine contractions to become excessive during the acute malarial attack. It has sometimes been urged that quinine should not be given in such large doses, or even at all, to a pregnant woman with malaria, on the theoretical ground that this drug itself increases uterine contractions and predisposes to abortion, but in practice it has been found by Mr. Edmonds and others that the greatest tendency to premature delivery is in the cases where no quinine is given, and it is emphatically urged by those who have had experience that quinine should be given all the more on account of the conjunction of pregnancy with the malaria. It actually makes the uterine contractions less than they are in cases in which no quinine is given, and by diminishing the pyrexia and lessening the frequency of the attacks not only is the prognosis as regards the mother's life greatly improved, but also the chances that the child will be stillborn are very considerably diminished. It may be incidentally remarked that the infant is sometimes born with a greatly enlarged spleen though there is not yet any absolute proof that the child's blood may actually contain the *Plasmodium malariae* at the time of birth.

#### INFLUENZA AND PREGNANCY.

Influenza is a disease the severity of which is so variable in different seasons that its effects upon pregnant women in particular are difficult to gauge. The statistics show that the prognosis is much graver in times of widespread epidemic than it is in sporadic cases, but this applies equally to non-pregnant as to pregnant patients. Jacquennier,<sup>37</sup> as long ago as 1837, came to the conclusion that influenza was no more dangerous to pregnant women than to anybody else.



The type of the disease was different in those days, however, from what it is now, and Cazcaux regards it as likely to be detrimental to the child. The weakness that is left after the acute phase is past is apt to last even longer in the pregnant woman than it is in other persons, and therefore even if the pregnancy does not come to an untimely ending the child is very apt to be born with deficient vitality and a tendency to die young. Lambinon<sup>38</sup> regards the bronchitic or pneumonic form of influenza as the most grave as regards both the mother and the child; but all observers agree that nothing is to be gained by interfering with the pregnancy, and the treatment should be, first, prophylactic in times of epidemic; and, secondly, that of extremely careful medical supervision should the disease be contracted in spite of all precautions taken to avoid it.

During an epidemic of influenza in Paris M. Bar and M. Bouillé<sup>39</sup> carefully watched the effects of the disease in 40 pregnant women. One of these had the nervous, 2 the gastro-intestinal, and 37 the respiratory form of the disease. Four of the latter developed influenzal pneumonia, 2 recovering slowly after delivery, 1 dying a few hours, and 1 on the third day after the child was born. The prognosis as regards the mother is, therefore, grave in the pneumonic type of influenza, but as regards the course of the pregnancy itself these observers came to the conclusion that it was not affected even if the influenza was severe.

#### LOBAR PNEUMONIA DURING PREGNANCY.

As regards ordinary lobar pneumonia in a pregnant woman, exclusive of pneumonia developing during the puerperium, the cases that have been in Guy's Hospital point to the following conclusions:—1. *If the pneumonia occurs early in the pregnancy*, the prognosis as regards the mother is little, if any, worse than it is in other patients of the same age. As regards the pregnancy, there is a probability that abortion will take place in about one-third of the cases, whilst in two thirds of the cases there is a likelihood not only that the mother will recover completely, but also that the child will be born living and healthy at term. 2. *If, on the other hand, the pneumonia develops during the second half of pregnancy*, the probability is that the latter will be then terminated in two-thirds of the cases, and the chances of the mother surviving will be greatly diminished, nearly half the patients dying if the pneumonia sets in after the sixth month. In other words, the more advanced the pregnancy the greater is the probability of an expulsion of the fetus and the graver the prognosis for the mother. Dr. Hirst<sup>40</sup> found that out of 43 cases of lobar pneumonia in pregnant women, 28 were less than six months pregnant and of these 11 aborted; of the 15 who were more than six months pregnant 10 aborted, and of these 15 mothers 7 died.

The question might be asked: Seeing that the prognosis as regards the child is in any case grave, might it not be wise to counsel termination of the pregnancy for the mother's sake if pneumonia sets in? The answer is definitely, No. Matton<sup>41</sup> records that out of 38 cases of pneumonia during pregnancy labour was induced in 18, and 9 of these patients died—a mortality of 50 per cent.; whereas of the 20 cases left to themselves only 1 died. These figures are not very new, and in interpreting them it must be remembered that labour would probably be induced chiefly in the worst cases, so that the high mortality cannot be entirely attributed to the treatment; but it is clear that the chances of the patient's recovery are at any rate not increased by interfering with the pregnancy, so that the right course to pursue is to treat the patients exactly as if they were not pregnant, unless Nature itself makes obstetric assistance necessary.<sup>42</sup>

It is wonderful how much illness a patient, even though she be pregnant, can pass through and yet recover from. Dr. Francis Hawkins,<sup>43</sup> for instance, records a case of a lady, aged 35 years, who, when four months pregnant, developed double lobar pneumonia, followed by endocarditis, severe bronchitis, acute dilatation of the heart, and finally by empyema. The pregnancy continued up to the sixth week after the onset of the illness, and had it not been for the empyema it would apparently have continued to term. The empyema was treated in the usual way, by rib resection, and ultimately, after a long illness of extreme severity, the patient got perfectly well.

Another case<sup>44</sup> illustrates the possibility of good results in spite of a grave prognosis. The patient was 38 years of age, and when eight and a half months pregnant she was seized with lobar pneumonia in the left lung. She was extremely ill. The crisis came on the seventh day, but very shortly afterwards she was as dyspnoeic as ever and the temperature rose again. A week after the crisis pus was located in the left pleural cavity and 34 oz. of it were drawn off by aspiration. It was hoped that rib resection might be avoided, but three days later it was necessary to give chloroform and drain the empyema. The patient was now at full term, and a few hours after the operation a strong healthy child was born, labour being easy and convalescence uneventful.

The pneumococcus may cause other lesions than pneumonia in a pregnant woman, but there is little evidence to show that the association is not due to chance. Vinay,<sup>45</sup> for example, records the case of a woman who, having suffered from great gastric irritability throughout her pregnancy, developed multiple subcutaneous abscesses during the seventh month. The pus gave cultures of pneumococci. The patient made a long struggle, but ultimately died nineteen days after delivery. There was nothing in this case to show that the pregnancy was in

any way directly concerned as a causal factor in the pneumococcal infection.

#### ADDISON'S DISEASE AND PREGNANCY.

We may now pass on to quite a different class of illnesses in the mother.

Addison's disease in conjunction with pregnancy is necessarily rare. There seem to have been only two cases of the kind in Guy's Hospital in the last 20 years, and both patients died. It is always very difficult to give an accurate prognosis in any case of Addison's disease, patients often dying almost suddenly when there has been no objective alteration in their general state for months previously. Consequently it is not possible to say that it was the pregnancy that hastened the end in these two cases. Nevertheless, the impression left upon one's mind is that the added strain of pregnancy was the immediate cause of death, and that pregnancy is therefore a very bad thing for a patient who has Addison's disease.

There is another point to mention, and that is the possible difficulty in diagnosis. Pregnancy itself may cause considerable increase in the pigment of the patient's skin, and the symptoms of weakness, vomiting, and even syncope may be attributed to the pregnancy itself in a case in which the pigmentation is not extreme, and in which the buccal mucosa has not been examined in a good light.

The two cases mentioned above were so similar to one another in most respects that the following notes of one of them may be taken to apply to both. The patient was 40 years of age, had had eleven children, the last two and a half years previously, and she was now five and a half months pregnant. She had begun to suffer from weakness, syncopal attacks, and undue pigmentation of the skin and buccal mucosa six months before she became pregnant, and Addison's disease had been diagnosed. At first the symptoms were not greatly increased by the pregnancy, but from the fourth month onwards the patient became distinctly weaker; attacks either of vomiting or syncope became so frequent that obstetric measures for terminating the pregnancy were adopted in the middle of the sixth month. The pulse-rate rose rapidly after delivery, and the heart's action became very feeble. There were several ill-defined convulsive seizures, and death occurred two days after labour. It may be mentioned that treatment by adrenalin had been pursued. At the necropsy both suprarenal capsules were typically caseous, and there was no other macroscopic disease.

#### LEUKAEMIA AND PREGNANCY.

Turning now to leukaemia, the cases may be divided into the acute and the chronic; and these are almost synonymous with the lymphatic and the spleno-medullary varieties. The acute form ends so rapidly in any case—usually within a few months of its first symp-



toms—that pregnancy is not at all likely to arise in a person who already has the disease. Acute leukaemia may, however, develop in a woman who is pregnant, and the summary of what then happens is that, bad though the prognosis is in other cases, the conjunction of pregnancy with the disease makes it still worse. Whether the association is accidental or whether something anomalous about the pregnancy may perhaps cause the leukaemia, it is hardly possible to say; but, judging from the rarity with which the two are associated, their conjunction would seem to be accidental. Hilbert<sup>46</sup> records the case of a woman, aged 37 years, who had been perfectly well up to the eighth month of her eighth pregnancy. She then complained of severe headaches, diarrhoea, fever, and gingivitis. Rhinitis and purpura followed, and blood examinations indicated typical lymphatic leukaemia. The pregnancy continued to the ninth month, when a macerated child was born spontaneously. The mother died from complete exhaustion ten hours after the labour and a little more than a month from the onset of her symptoms.

Spleno-medullary leukaemia, on the other hand, may last for three or four years after the first symptoms lead to its diagnosis, and pregnancy may arise in a patient who is already known to have the disease. Dr. Herman<sup>47</sup> has recorded one such case and has collected altogether seven undoubted others. Owing to the enlarged spleen pregnancy gave much more abdominal distension than normal; in some cases, indeed, it is wonderful how both the huge spleen and a full-term pregnancy can be included in the same abdomen. It is not surprising that there is a great tendency to premature delivery. The puerperium is a very dangerous time, some of the patients dying very soon after the termination of the pregnancy, though if the patient survives the particularly dangerous time that immediately follows delivery considerable temporary improvement in her general health is to be expected. Dr. Herman concludes that pregnancy does nothing but harm to a leukaemic patient, and recommends that it should be artificially terminated as soon as possible.

It would be very interesting to know whether the children of leukaemic patients are ever born with enlarged spleens similar to the enlargement of that organ sometimes found in the offspring of parents suffering from malaria.<sup>48</sup> It would also be interesting to know what effects upon the pregnancy repeated applications of the *x* rays to the maternal abdomen would have. There are no statistics upon the subject. Evidence is accumulating to show that *x*-ray applications may be very efficient in diminishing the size of the spleen and in ameliorating the symptoms for the time being in cases of splenomedullary leukaemia. If it were known that their application to the splenic region in the mother had no ill effect upon the child, it might be well to advise leaving the pregnancy to run its course whilst

the leukaemia was simultaneously being treated with the *x* rays. In the absence of evidence either way, however, it would seem likely that the *x* rays would do harm to the child, in which case, rather than risk the mother's life unnecessarily, the right course to advise would seem to be to have the pregnancy terminated as soon as possible, and then to adopt the *x*-ray treatment if it still seemed good to do so.

#### DIABETES MELLITUS AND PREGNANCY.

Diabetes mellitus in conjunction with pregnancy has many points of interest. There has been much discussion as to the nature of the reducing bodies that are often present in the urines of pregnant women, especially in the later months. There is no doubt that lactose is commonly present, both towards the end of pregnancy and during the puerperium; but it seems equally clear that a considerable proportion of pregnant women have actual glycosuria.

Saleim,<sup>49</sup> as the result of careful examinations, states that two-thirds of all pregnant women pass increased quantities of glucose in this way. This glycosuria of pregnancy causes no symptoms, however, and it disappears without treatment. It seems, therefore, to bear no relationship to diabetes mellitus itself. Nevertheless, seeing that pregnancy thus predisposes to glycosuria, and seeing that, if they can become pregnant, the patients who are suffering from this complaint must necessarily be comparatively young, and therefore predisposed to the worst form of diabetes mellitus, it might well have been expected that pregnancy would be very harmful if it occurred in a patient already suffering from diabetes mellitus. It is difficult amongst hospital cases to be sure that the glycosuria has antedated pregnancy, and only two clear instances of the kind have occurred in Guy's Hospital lately. One of these patients was a very stout woman, aged 36 years, whose pregnancy went naturally to term, although her urine was loaded with sugar, and also contained both diacetic acid and acetone in abundance. The other was a younger woman, aged 23 years, whose urine also contained sugar, diacetic acid, and acetone, and whose pregnancy ran a perfectly normal course, ending in the birth of a healthy child at term. In both these cases there was a large excess of liquor amnii; this has been noticed by several observers as being almost characteristic in the case of diabetic mothers, and the amniotic fluid often contains sugar.

It is not every case that passes through pregnancy with as little trouble as the above. Ludwig,<sup>50</sup> for example, records a severe case in which a woman, aged 42 years, was in her ninth pregnancy. Marked diabetes mellitus had existed for two and a half years, but she had reached the last month of this pregnancy without any trouble beyond pruritus vulvae. The abdomen now became suddenly larger and the patient was admitted to hospital very ill, semi-conscious, with abundance of sugar, diacetic acid, and acetone in her urine. Labour was induced, nine

pints of liquor amni escaping. The fetus was in an advanced state of maceration. The patient was very ill for two days afterwards, but she slowly recovered, though her diabetes persisted as before. It is interesting to note that the hydramnios occurred suddenly in this case; and it is also noteworthy that the fetus was macerated, for it may have been on this account that the mother was so ill.

The general conclusions that other recorded cases<sup>61</sup> point to are: That diabetes mellitus is by no means incompatible with pregnancy; that cases of moderate severity are not made materially worse by pregnancy; and that there seldom seems to be any reason for interfering with the pregnancy.

Some observers<sup>62</sup> have even stated their opinion that pregnancy, instead of making the diabetes worse, actually ameliorates it for the time being—a point of great interest when one recalls the effects of typhoid fever, for example, in similar cases. A patient with diabetes mellitus may develop typhoid fever, and during that illness the glycosuria may entirely cease, returning again when the fever subsides.

#### DIABETES INSIPIDUS AND PREGNANCY.

Diabetes insipidus is a condition which may actually arise during pregnancy as a result of a severe mental shock at that time. Should it do so, it seems that it does not go away again after the child is born. It may also have existed previously to pregnancy. The chief trouble to the patient is the fact that when the uterus enlarges there is less room for the bladder; micturition becomes annoyingly frequent and acute retention of urine is apt to occur if micturition is postponed. Sleep may become very broken in consequence of this and also because of the constant necessity for drinking water or other liquid. The pregnancy itself runs no abnormal course, the children may be perfectly healthy, and there is no marked tendency to hydramnios with its inordinate abdominal distension such as occurs in diabetes mellitus.

There seems to have been no case of extreme diabetes insipidus in association with pregnancy in Guy's Hospital, but in one medium case the patient a very stout woman, was passing up to 15 pints of limpid urine daily, of specific gravity 1003. The water alone was increased, the total solids being normal. In this instance the polyuria and polydipsia had not been present until the middle of the fifth pregnancy, when these symptoms came on suddenly after a severe fright. If the patient failed to micturate directly the desire came she developed retention of urine, necessitating the use of a catheter, and on some such occasions the bladder contained as much as four pints at a time. The child was born normally, but the polyuria and polydipsia persisted.

Cases of diabetes insipidus in association with pregnancy have been recorded by Bennett, Matthews Duncan, Esterle, Merbach, Kleinwachter, Vinay,<sup>63</sup> and others. The two following may be mentioned in particular because they



are instances of diabetes insipidus developing from mental shock and because they show that although the diabetes insipidus does not seem to be in itself dangerous the patients are apparently more liable than others to contract, and die from, intercurrent maladies of the lungs.

One patient was a woman, aged 32 years, who kept a farm. When she was pregnant a flood destroyed all her crops, and immediately after this severe mental shock, polydipsia and typical diabetes insipidus set in. The patient passed up to 5½ gallons of urine daily, yet became pregnant for the second time. During the pregnancy the polyuria abated somewhat, the least quantity of urine passed in one day being 9 pints. Delivery was normal; thereafter the urine at once increased in quantity again, but the patient left the hospital otherwise in good health. Shortly afterwards, however, she died from double pneumonia.

The second patient was a woman, aged 26 years, who was four months pregnant for the fifth time when a fire destroyed her house and all she possessed. Diabetes insipidus set in directly, 20 pints of almost pure water passing daily; the total solid constituents of the urine were normal. Labour occurred normally at term, but the child was sickly and died in two weeks. The patient continued to have polyuria; she developed phthisis and died 19 months after the fire.

#### MYXOEDEMA AND PREGNANCY.

There do not seem to be many recorded cases of pregnancy in patients suffering from myxoedema. Apparently this disease is not incompatible with conception, at any rate in persons who are receiving thyroid treatment. In the one case observed by me the pregnancy had no ill-effect upon the mother's condition, and if it had not been for the accident that her pelvis was much contracted, there seems to be no reason why she should not have borne children naturally. As regards the child, the main danger is that it will have a deficient thyroid gland and be a cretin, unless upon the first suspicion of this, treatment with some preparation of thyroid gland is begun. The patient in question was 40 years of age and enormously stout. She had been receiving thyroid treatment for her myxoedema for over two years. Her pregnancy went to full term and natural labour came on, but there were great obstetrical difficulties which need not be recounted. The recuperative power of the patient, notwithstanding her myxoedema, is evidenced by the fact that she ultimately got quite well in spite of long continued sapraemia and a "white" arm due to thrombosis of the right axillary vein.

There is no time left for the discussion of a number of other conditions that one would like to enter upon, such as the effects of pregnancy upon Graves's disease, upon ordinary goitre, upon malignant disease, upon phthisis, upon heart disease, upon chorea, and upon many other

things which are full of interest. The varieties of jaundice that may occur during pregnancy might form a chapter by themselves. There is a whole group of cases in which a pregnant woman dies and nothing very abnormal is found at the *post mortem* examination to account for her death. It is with regret that one is obliged to leave out these for want of time. My views have already been expressed about some of them elsewhere,<sup>5,4</sup> however; and if I may be pardoned for making one more remark it is in connexion with chorea gravidarum.

#### CHOREA AND PREGNANCY.

Mr. H. T. Hicks and myself<sup>55</sup> have expressed the view that "'simple' chorea gravidarum is to fatal chorea gravidarum as 'simple' endocarditis is to fungating endocarditis," and that the violence of the choreic movements is not of nearly so great importance in estimating the prognosis as is the presence or absence of pyrexia. Out of 29 consecutive cases of the disease at Guy's Hospital, 26 patients recovered and 3 died. In none of the 26 cases of recovery was there any material pyrexia, although in some of the cases the movements were very violent; in the cases that died, on the other hand, there was marked pyrexia in every instance. There will doubtless be exceptions, but, as a broad rule, we suggest that, provided the temperature remains almost normal, as in Chart 3, the prognosis is good even if the movements are very violent; whereas if the chart shows marked pyrexia, uninfluenced by salicylates, as in Charts 4 and 5, the prognosis is very grave, provided no obvious cause—such as pleurisy, acute tonsillitis, and the like—can be found to account for the fever. It will be very interesting to see whether other observers will find this to hold good in future cases that may come under their notice.

I thank you, Mr. President and gentlemen, for listening so patiently to these lectures, and I will conclude by reverently recalling to your thoughts the name of their founder, Dr. Goulston.

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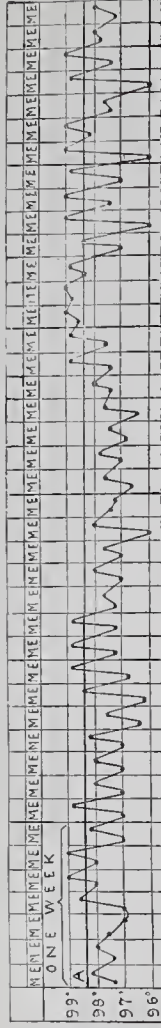


Chart 3.—Chorea and pregnancy. Movements violent. No pyrexia. Recovery. A, On admission.

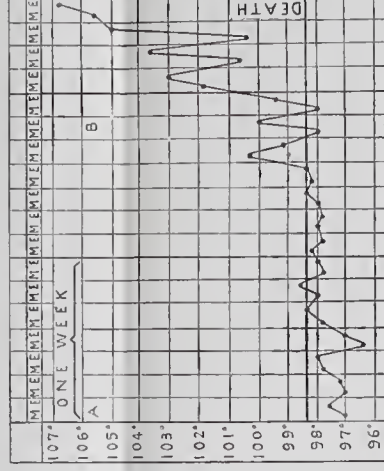


Chart 4.—Chorea and pregnancy. Pyrexia. Death.  
A, On admission B, Accouchement forcé.

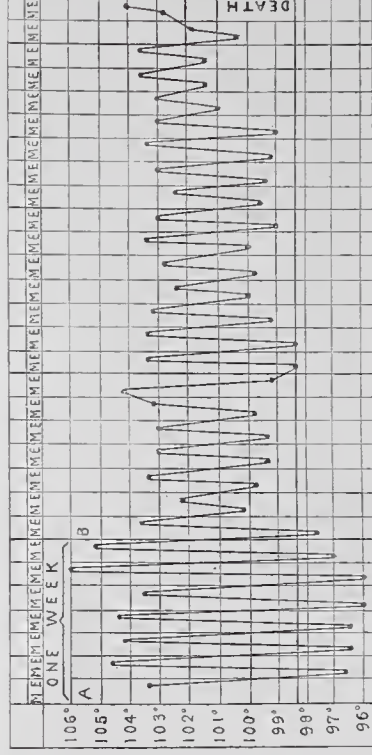


Chart 5.—Chorea and pregnancy. Prolonged and severe pyrexia. Death. A, On admission. B, Spontaneous premature delivery.





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